

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

|  |   |   |
|--|---|---|
| Applicant's or agent's file reference<br><b>4239-55911</b>             | <b>FOR FURTHER ACTION</b>                                       | see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. |
| International application No.<br><b>PCT/US 00/ 26689</b>               | International filing date (day/month/year)<br><b>29/09/2000</b> | (Earliest) Priority Date (day/month/year)<br><b>02/10/1999</b>  |
| Applicant<br><b>THE GOVERNMENT OF THE UNITED STATES OF AMERICA, as</b> |   |   |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

- the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  **Certain claims were found unsearchable** (See Box I).

3.  **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

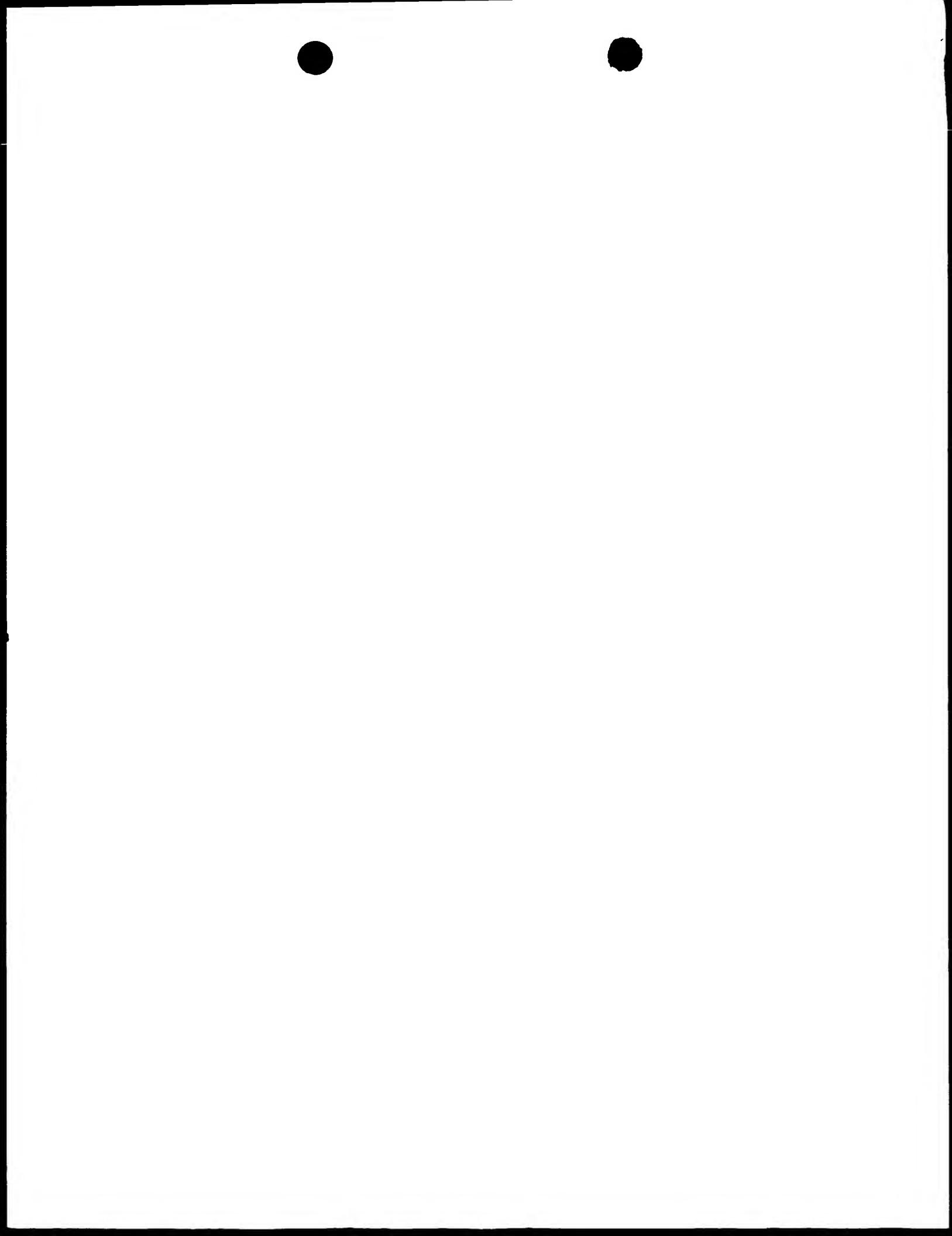
5. With regard to the **abstract**,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.



FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 1-26, 37-41 and 27-32, as far as they refer to an invivo method, are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Although claims 33-36 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.2

Present claims 1-5, 17, 20-21, 23, 25-26, 33-38 relate to a compound defined by reference to a desirable characteristic or property, namely modulation of FGF-5 expression/activity or modulation of immune response to FGF-5.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the use of FGF-5 polypeptides, nucleic acids encoding FGF-5, FGF-5 antisense molecules, antibodies to FGF-5 and immunoreactive sensitized T cells sensitized with FGF-5.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.



## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 00/26689

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A61K38/18 C07K14/50 A61K39/395 C07K16/22

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No   |
|----------|---|--|
| X, P     | WO 00 24756 A (HUNAN GENOME SCIENCES INC.)<br>4 May 2000 (2000-05-04)<br>claims 1-23<br>---<br>WO 99 55861 A (EISAI CO. LTD.)<br>4 November 1999 (1999-11-04)<br><br>claims 1-19,23,24<br>page 42, line 10 - line 3<br>page 46, line 20 -page 47, line 26<br>---<br>WO 90 12597 A (THE SALK INSTITUTE FOR<br>BIOLO) 1 November 1990 (1990-11-01)<br>the whole document<br>--- | 1-41<br><br>1-5,<br>9-14, 23,<br>24,<br>27-32,<br>37-40<br><br>1-6, 23,<br>24, 37-39 |
| X        | -/-   |  |



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## ° Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- \*g\* document member of the same patent family

Date of the actual completion of the international search

9 July 2001

Date of mailing of the international search report

20/07/2001

Name and mailing address of the ISA  
European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel (+31-70) 340-2040, Tx. 31 651 epo nl.  
Fax (+31-70) 340-3016

Authorized officer

Siatou, E



## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 00/26689

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication where appropriate, of the relevant passages   | Relevant to claim No. |
|----------|---|-----------------------|
| X        | PATENT ABSTRACTS OF JAPAN<br>vol. 1998, no. 05,<br>30 April 1998 (1998-04-30)<br>& JP 10 017599 A (POLA CHEM IND INC),<br>20 January 1998 (1998-01-20)<br>abstract<br>---   | 33-36                 |
| A        | ZHAN X ET AL: "THE HUMAN FGF-5 ONCOGENE<br>ENCODES A NOVEL PROTEIN RELATED TO<br>FIBROBLAST GROWTH FACTORS"<br>MOLECULAR AND CELLULAR<br>BIOLOGY, US, WASHINGTON, DC,<br>vol. 8, no. 8, 1 August 1988 (1988-08-01),<br>pages 3487-3495, XP002034597<br>ISSN: 0270-7306<br>abstract<br>---   | 1-41                  |
| A        | DATABASE EMBASE 'Online!<br>ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM,<br>NL;<br>YAMANAKA K. ET AL: "Expression of<br>fibroblast growth factors in human<br>non-papillary renal cell carcinoma:<br>Correlation with tumor progression."<br>retrieved from STN<br>Database accession no. 1999207619<br>XP002171451<br>abstract<br>& INTERNATIONAL JOURNAL OF CLINICAL<br>ONCOLOGY, (1999) 4/2 (74-77). ,<br>---           | 1-41                  |
| A        | DATABASE CHEMABS 'Online!<br>CHEMICAL ABSTRACTS SERVICE, COLUMBUS,<br>OHIO, US;<br>YOSHIMURA, KOJI ET AL: "Messenger<br>ribonucleic acids for fibroblast growth<br>factors and their receptor in bladder and<br>renal cell carcinoma cell lines"<br>retrieved from STN<br>Database accession no. 124:339650 HCA<br>XP002171452<br>abstract<br>& CANCER LETT. (SHANNON, IREL.) (1996),<br>103(1), 91-7 ,<br>---<br>-/- | 1-41                  |



## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/26689

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No. |
|----------|--|-----------------------|
| A        | <p>DATABASE CHEMABS 'Online!<br/>     CHEMICAL ABSTRACTS SERVICE, COLUMBUS,<br/>     OHIO, US;<br/>     WERNER, SABINE ET AL: "Fibroblast growth<br/>     factor 5 proto-oncogene is expressed in<br/>     normal human fibroblasts and induced by<br/>     serum growth factors"<br/>     retrieved from STN<br/>     Database accession no. 116:35063 HCA<br/>     XP002171453<br/>     abstract<br/>     &amp; ONCOGENE (1991), 6(11), 2137-44 ,</p> <p>-----</p> | 1-41                  |



## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/26689

| Patent document cited in search report |   | Publication date | Patent family member(s) |             | Publication date |
|--|---|------------------|-------------------------|-------------|------------------|
| WO 0024756                             | A | 04-05-2000       | AU                      | 4688499 A   | 15-05-2000       |
| WO 9955861                             | A | 04-11-1999       | AU                      | 3170499 A   | 16-11-1999       |
| WO 9012597                             | A | 01-11-1990       | US                      | 5191067 A   | 02-03-1993       |
|  |   |                  | CA                      | 2053275 A,C | 28-10-1990       |
|  |   |                  | DE                      | 69010330 D  | 04-08-1994       |
|  |   |                  | DE                      | 69010330 T  | 20-10-1994       |
|  |   |                  | EP                      | 0470183 A   | 12-02-1992       |
|  |   |                  | JP                      | 2891306 B   | 17-05-1999       |
|  |   |                  | JP                      | 4507093 T   | 10-12-1992       |
|  |   |                  | US                      | 5576288 A   | 19-11-1996       |
|  |   |                  | US                      | 5679637 A   | 21-10-1997       |
| JP 10017599                            | A | 20-01-1998       | NONE                    |             |                  |



**INTERNATIONAL SEARCH REPORT**International application No.  
PCT/US99/13620**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-12, 14-16

**Remark on Protest**

- The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/13620

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claims 1-12 and 14-16, drawn to nucleic acid, vector, host cell, polypeptide, methods of making host cell and polypeptide.

Group II, claim 13, drawn to an antibody.

Group III, claim 17, drawn to a method of administering a polypeptide.

Group IV, claim 18, drawn to a method of diagnosis relating to mutations in DNA.

Group V, claim 19, drawn to a method of diagnosis relating to the expression of a polypeptide.

Group VI, claim 20, drawn to a method for identifying binding partners for a polypeptide.

Group VII, claims 21, 22 and 23, drawn to a method for identifying compounds which modulate the cellular response induced by FGFR5.

The inventions listed as Groups I-VII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: This Authority considers that the main invention in the instant application comprises the first-recited product, polynucleotide encoding FGFR5, and the first-recited method of using that product, namely in the process of producing the encoded polypeptide. Note that there is no method of making the polynucleotide. Also included in this group is the product made, namely the encoded polypeptide, and vector and host cell comprising the polynucleotide. Further, the ISA/US considers that the materially and functionally dissimilar product of group II and the additional methods of groups III-VII do not correspond to the main invention. This Authority therefore considers that the several inventions do not share a special technical feature within the meaning of PCT Rule 13.2 and thus do not relate to a single general inventive concept within the meaning of PCT Rule 13.1.

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|     |  |     |
|-----|--|-----|
| 1   | CAGGCCAGGTCCCGACAGCAGGAGATGAGGCCAGCCCCCTGTTGGCTGCCTGGCTGGCG        | 60  |
| 1   | M T P S P L L E L L L P  | 12  |
| 61  | CCCCTGGCTGGCGGCGCTTCCCACCGGGCGGCCCGCGCGAGGGCGGGAAAGATGGCG          | 120 |
| 13  | P L L L G A F P P A A A A R G P P K M A                            | 32  |
| 121 | GACAAGGTOCTCCCACGGCACGGTGCCCGGCGCTGGGCCCGACTGTGGCCCTGGCACTGCCA     | 180 |
| 33  | D K V V P R Q V A R L G R T V R L Q C P                            | 52  |
| 181 | GTCGAGGGGGAGCGCGCGCGCGCTGACCATGTCGACCAAGGAAGGATGGCGGCCACCATCCACAGC | 240 |
| 53  | V E G D P P P L T M W T K D G R T I H S                            | 72  |
| 241 | GGCTGGAGCCGCTTCCCGCGCTGGCTCCCGCAAGGGCGCTGAGGTGAAGCAGGTGGAGGGAG     | 300 |
| 73  | G W S R F R V L P Q G L K V K Q V E R E                            | 92  |
| 301 | GATGCCCGGCTGTAAGCTGCAAGGCCACCAACGGCTTGGCAGGCCCTAGCGTCAACTAC        | 360 |
| 93  | D A G V Y Y C K A T N G F G S L S V N Y                            | 112 |
| 361 | ACCCCTCGTGTGGATGACATTAGCGAACGGAGAGGAGCCCTGGGCCCGAGACAGCTCC         | 420 |
| 113 | T L V V L D D I S P G K E S L G P O S S                            | 132 |
| 421 | TCTGGGGCTCAAGAGGACCCCGGCCAGCCAGTAGGGCAGCGACCGCGCTTCACACAGCCC       | 480 |
| 133 | S G G Q E D P A S Q Q W A R P R F T Q P                            | 152 |
| 481 | TCCAAGATGAGGGCGCCGGGTGATCGCACGGCCCGTGGTAGCTCCGTGGCGCTCAAGTGC       | 540 |
| 153 | S K M R R R V I A R P Y G S S V R L K C                            | 172 |
| 541 | GTGGCCAGCGGGCACCCCTGGCGGACATCACGTGGATGAAGGAGGACCGCCCTGGACC         | 600 |
| 173 | V A S G H P R P D I T W M K O D Q A L T                            | 192 |
| 601 | GGCCCAGAGGCCGCTGAGCCACGGAGAGAAGAAGTGGACACTGAGCCTGAAGAACCTGG        | 660 |
| 193 | R P E A A E P R K K K W T L S L K N L R                            | 212 |
| 661 | CGGGAGGACAGGGCAAATACACCTGGCGGCGCTGTCGAACCGGGGGCGCCATCAAGGCC        | 720 |
| 213 | P E D S G K Y T C R V S N R A G A I N A                            | 232 |
| 721 | ACCTAGAAGGTGGATGTGATCCAGCGGACCGCTTCCAAACCGCGCTGCTCACAGGACGGCAC     | 780 |
| 233 | T Y K V D V I Q R T R S K P V L T G T H                            | 252 |
| 781 | CCCGTGAACACGGADGGTGGACTTCCGGGGACCAAGFCCTTCCAGTGGCAAGGTGGCGAGC      | 840 |
| 253 | P V N T T V D F G G T T S F Q C K V R S                            | 272 |
| 841 | GAAGTGAAGCGGTGATCCAGTGGCTGAAGCGCGTGGAGTACGGCGGGAGGGCGAC            | 900 |
| 273 | D V K P V I Q W L K R V E Y G A E G R H                            | 292 |
| 901 | AACTCCACCATCGATCTGGCGGCCAGAGTTTGTGGCTGCCACGGGTGACGTGTGG            | 960 |
| 293 | N S T I D V G C Q K F V V L P T G D V W                            | 312 |

FIG. 1A

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|      |  |      |
|------|--|------|
| 961  | TGCGCCGCCGADCGCTTCACTCAATAAGCTGCTCATCACCGGTGGCGGCCAGGAAGAT     | 1020 |
| 313  | S R P D G S Y L N K L L I T R A R Q O D                        | 332  |
| 1021 | CGGGGCATGTAACATCTGCCCTGGGCCAGACCATCGGCTACAGCTTCGGCAAGGGCTTC    | 1080 |
| 333  | A G M Y I C L G A N T M C Y S F R S A F                        | 352  |
| 1081 | CTCACCGTCTGCCAGACCCAAAAAGGCCAAGGGCCACCTGTGGCCTTCTCGTGGCC       | 1140 |
| 353  | L T V L P D P K P Q G P P V A S S S A                          | 372  |
| 1141 | ACTAGGCTGGCGTGGCGCTGGTCAATCGGCAATCCCAGGCCCCCGCTCTTCATCCTGGCC   | 1200 |
| 373  | <u>T S L P W P V V I G I P A G A V F I L G</u>                 | 392  |
| 1201 | ACCCCTGCTCCCTGGCTTGCCAGGGGGAGAAGAACCGCTGGCACCCCCCGCGCGCTGGCGCT | 1260 |
| 393  | <u>T L L L W L C Q A Q K K P C T P A P A P</u>                 | 412  |
| 1261 | CCCGCTGGCTGGGCCACGG  | 1320 |
| 413  | P L P G H R P P G T A L D R S G D K D L                        | 432  |
| 1321 | CCCTCGTTGGCGCGCTCAGGGCTGGCCCTGGTCTGGGGCTGTGTGAGGAGGAGATGGCTCT  | 1380 |
| 433  | P S L A A L S A G P G V G L C E E H G S                        | 452  |
| 1381 | CCGGCAGGCCCCAGCACTTACTGGGCCAGGGCCAGTTGCTGGCCCTAACITCTACCC      | 1440 |
| 453  | P A A P Q H L L G P G P V A G P K L Y P                        | 472  |
| 1441 | AAACTCTACACAGACATCCACACACACACACACACTCTCACACACACTCACACGTG       | 1500 |
| 473  | K L Y T D I H T H T H T H S H T H S H V                        | 492  |
| 1501 | GAGCGAACGCTAACCGAACATCCACTATCAGTGGTAGAGGGACCGTATCTGGCACTGG     | 1560 |
| 493  | E G K V H Q H I H Y Q C *                                      | 505  |
| 1561 | GCACGGGGGGGGGGGGAGACAGGGAGACTGGAGGATGGAGGACGGAGCTCCAGACGAA     | 1620 |
| 1621 | GGCACGGGACCCATGGCGAGGAGGAATGGCCAGGACGGAGGACTGTGTGAGGGCA        | 1680 |
| 1681 | TAGCCCCCTGGACACACACACAGACACACACACTACCTGGATCCATGTATCCACACACA    | 1740 |
| 1741 | TGGGGCACACGTGCTTGGAGGCACACGTAGGCACACACGGCACATGGCACAGATATGC     | 1800 |
| 1801 | CGGCTGGGCACACAGATAAGCTGGCAAATGGCAOGCACAOGGCACAGAGACATGGCACAC   | 1860 |
| 1861 | ATACAAGGACATGCTGGCTGAACATACACACGGCACACCCATGGCAGATGTGCTGGCTCG   | 1920 |

FIG. 1B

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|      |  |      |
|------|--|------|
| 1921 | ACACACACACACACACACGGATATGCTGTCGGACGCACACACGTCCAGATAATGGTATCCG        | 1980 |
| 1981 | ACACACACGTGCACAGATAATGCTGCCCTGGACACACAGATAATGCTGCCCTTGACACACACA      | 2040 |
| 2041 | TGGCAACGGATATTGCCCTGGACACACACACACACACACACGGGTTGCACAGATAATGCTGTCGGAGA | 2100 |
| 2101 | GGCACACACATGCAGATAATGCTGCCCTGGACACACACACTTCCAGACACACACGTGCACAGCGC    | 2160 |
| 2161 | AGATAATGCTGCCCTGGACACACGGAGATAATGCTGCTCTAGTCACACACACACGGAGACATGC     | 2220 |
| 2221 | TGTGGGACACACACACACACGGCATCCACAGATAATGCTGTCGGACACACACACACGGCAAGCAGAT  | 2280 |
| 2281 | ATGCTGCCCTGGACACACACACAGATAATGCTGCCCTAACACTCACACACADGTGCAGATAATT     | 2340 |
| 2341 | CCCTGGACACACACATGTGCACAGATAATGCTGCTCTGGACACATGGCACACACGGTGCAGATAATG  | 2400 |
| 2401 | CTGTGGGATAACACADGGACCCACACATGGAGATAATGCTGCCCTGGGACACACACTTGGGA       | 2460 |
| 2461 | CACACATGCACACACAGGGGGAGATAATGCTGCCCTGGACACACGGCAGACTGACGTGGTTT       | 2520 |
| 2521 | GGGAGGGTGTGCCGTGAAGGCTCCAGTAAGTGTGCCGTGAGGCTCATAGTTGATGAGGG          | 2580 |
| 2581 | CTTTCGCTGCTCCACCGTCACTCCCCAACTCTGGGGGCTCTGTCCCCGGCTCACTCC            | 2640 |
| 2641 | GGGTGCGATGCCCGCCTCTGTCGGGCTGGGGCTATTTTGCCACCTGCCCTGG                 | 2700 |
| 2701 | TCCCGACGGAGTCCGCTACTGCTGTGGCTGGGGTGGGGGGGGACAGCAAGGGCAAGGCTGA        | 2760 |
| 2761 | GAAGCTGGAGCCCATGGCTAGTGGCTCATCCCCACTGGATTTCTCCCCCTGACACAGAGAA        | 2820 |
| 2821 | GGGGCCTGGTATTTATTTAAGAAATGAAGATAATATTAATAATGATGGAAGGAAGAC            | 2880 |
| 2881 | TGGGTTGCACGGACTGTGGCTCTCTGGGGCCGGGGACCCGGCTGGCTTTCAAGCCATG           | 2940 |
| 2941 | CTGATGACGACACACCGTCCAGGGCAGACACCAACCCCGACCCGACTGTGGTGGGG             | 3000 |
| 3001 | CAGATCTCTGTAATTATGAGAGTTTGAGCTGAAGGCCCCGTATATTAAATTATTTG             | 3060 |
| 3061 | TTAAACATGAAAGTGCATCCCTTCCCTCCAAAAAAA 3112                            |      |

FIG. 1C

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|      |  |     |                                  |     |            |
|------|--|-----|----------------------------------|-----|------------|
| 1    | ITPSP - LLL - PFLL GAF PFAAARGP - - - - -                        | 20  | PKMAKDVYVPRQPAFLEERTYR - - - - - | 40  | FGFR5 prot |
| 1    | R - - - - -  | 50  | PLSLEASSEEVLEPCLA - - - - -      | 70  | FGFR4prot  |
| 51   | TPVE DOPPLTMATKESRTIHSSGWSSFF YLPQSI KVKQVERE DAEVWFKSTINGSGSLSV | 80  | 100                              | 120 | FGFR5 prot |
| 57   | C - - - - -  | 140 | 160                              | 180 | FGFR4prot  |
| 111  | TY I VVYL JQISPGKESLIGEDSSGGQEDPASQ - - - - -                    | 150 | 170                              | 190 | FGFR5 prot |
| 112  | EL - LITG ISLTSSNDDEDKSHDPSNRHSSYP - - - - -                     | 160 | 180                              | 200 | FGFR4prot  |
| 1170 | LKEVQSSHHREFDUTAKMNDQAAPEAAEPFKKKQSTSLKNLRFECSKKNTRPSSR          | 210 | 220                              | 230 | FGFR5 prot |
| 1170 | FRCP2AENHTTTRALKEGAAFHGENHPIGGIRLTHQHQHQSIVMESYVUPSSR            | 240 | 250                              | 270 | FGFR4prot  |
| 196  | TGTHPVYVTTTVDFFGTTSFQCKYRSSEYKFSVQNLKRVET                        | 280 | 290                              | 300 | FGFR5 prot |
| 227  | A EATNATKVRQIQTBSKSYTGTTHPVYVTTTVDFFGTTSFQCKYRSSEYKFSVQNLKRVET   | 320 | 340                              | 350 | FGFR4prot  |
| 230  | Y ESSRYYNLLDPELERSPHRRIEQAGLPAQ - - - - -                        | 360 | 380                              | 400 | FGFR5 prot |
| 287  | GAEGRHNSTIDVGEGIKFY - - - - -                                    | 370 | 390                              | 410 | FGFR4prot  |
| 288  | - - - - -  | 430 | 450                              | 470 | FGFR5 prot |
| 346  | TSFRSAFL - - - - -   | 440 | 460                              | 480 | FGFR4prot  |
| 341  | LSYQSAWLL - - - - -  | 490 | 510                              | 530 | FGFR5 prot |

**SUBSTITUTE SHEET (RULE 26)**

EIG 24

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396 - E F P Q D R I V L S K P L G E G C F G Q W R E A F G M D S A R D Q S T Y A W X M L K D M A S O D K U R A D L V F G F S S p r o t

499 - S S E G P L S F P H L S A Y Q W A R G M Q V L E S R C I H R D A A R N V A T E D M A K I A D F L A B G H F G F S S p r o t

519 - S E K E V M A L I G R H K M I N L G V C T D E G P L Y V I W E C A K E G M L R E F L R A B P D P D S P D S R F G F S S p r o t

429 - F S L L R E G H M D R P H C P F E E G L M R E C H A A P S Q R T F K Q L V E A L D O K V L A Y S E L E R F G F F M p r o t

639 - I O A Y K T S W G R L P H K N N P E A L F O R Y I T H Q S U M S F G T I L A E L F T I - P K L T E I H F G F F M p r o t

488 - T H T H T H S H T H S H V E G K H Q D p l p l l s f p f G S 5 4 9 T F G P Y S P S S G D A S S T C S S S D S F S F G F F M p r o t

689 - L T F G P Y S P S S G D A S S T C S S S D S F S F G F F M p r o t

480 - T H T H T H S H T H S H V E G K H Q D p l p l l s f p f G S 5 4 9 T F G P Y S P S S G D A S S T C S S S D S F S F G F F M p r o t

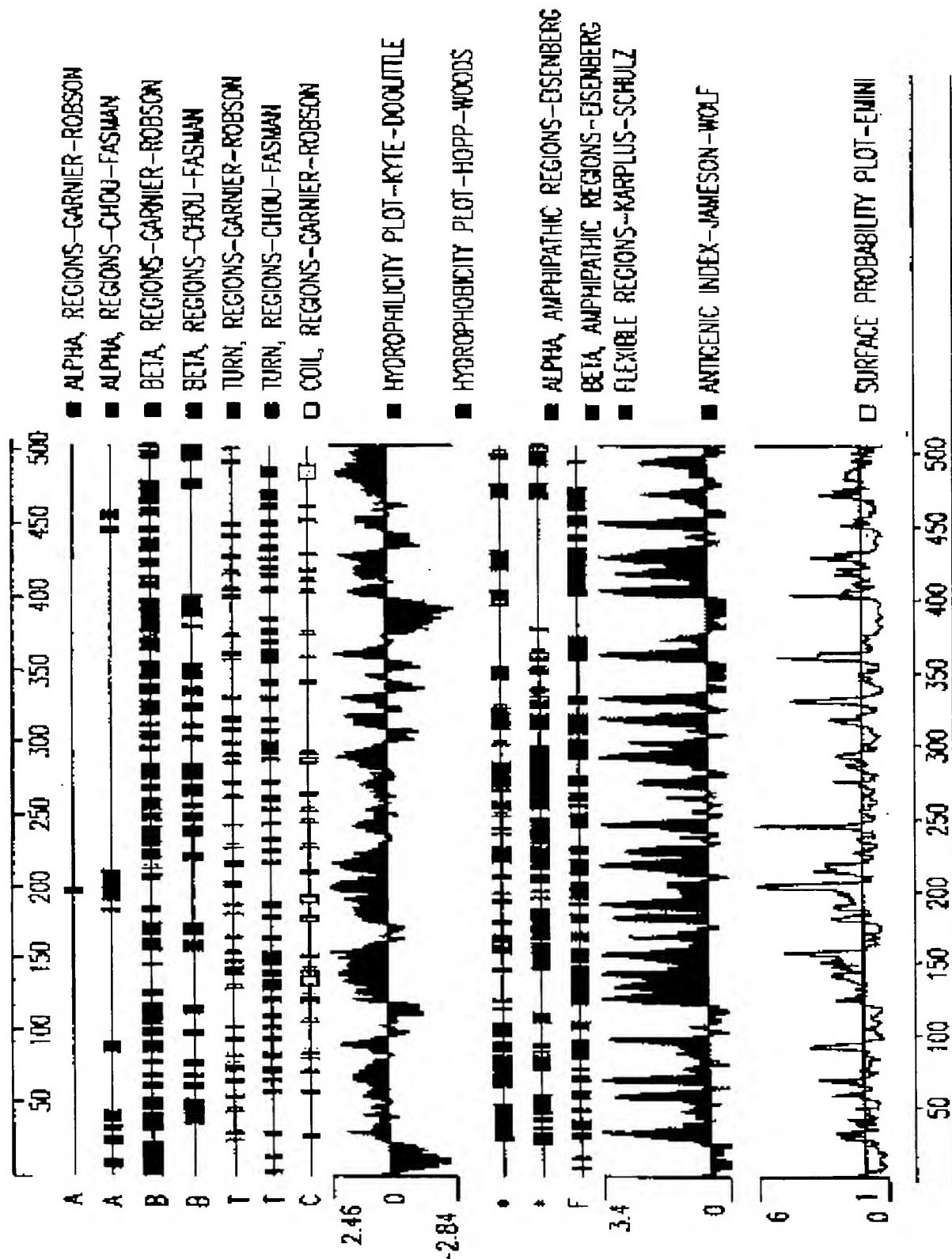
579 - F G F F M p r o t

340 - 490 500 510 520 530 540 550 560 570 580 590 600 610 620 630 640 650 660 670 680 690 700 710 720 730 740 750 760 770 780 790 800 810 820 830 840 850 860 870 880 890 900 910 920 930 940 950 960 970 980 990 1000

FIG. 2B

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FIG. 3



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| Res | Pos | Garni - Alpha | Chou - Alpha | Garni - Beta | Chou - Beta | Garni - Turn | Chou - Turn | Garni - Coil | Chou - Coil | Eisen - Alpha | Eisen - Beta | Korpi - Flexi | Jones - AntiG | Emini - Surfa - |
|-----|-----|---------------|--------------|--------------|-------------|--------------|-------------|--------------|-------------|---------------|--------------|---------------|---------------|-----------------|
| Met | 1   | -             | -            | -            | -           | -            | -           | -            | -           | 0.31          | -0.11        | F             | -0.05         | 1.11            |
| Thr | 2   | -             | -            | -            | -           | -            | -           | -            | -           | -0.53         | -0.53        | F             | 0.25          | 1.34            |
| Pro | 3   | -             | -            | -            | -           | -            | -           | -            | -           | -0.96         | -1.38        | F             | -0.20         | 0.87            |
| Ser | 4   | -             | -            | -            | -           | -            | -           | -            | -           | -1.53         | -2.09        | F             | -0.20         | 0.72            |
| Pro | 5   | -             | -            | -            | -           | -            | -           | -            | -           | -2.09         | -2.60        | F             | -0.05         | 0.41            |
| Leu | 6   | -             | -            | -            | -           | -            | -           | -            | -           | -2.60         | -2.60        | F             | -0.45         | 0.22            |
| Leu | 7   | -             | -            | -            | -           | -            | -           | -            | -           | -2.60         | -2.60        | F             | -0.60         | 0.14            |
| Leu | 8   | -             | -            | -            | -           | -            | -           | -            | -           | -2.60         | -2.60        | F             | -0.60         | 0.07            |
| Leu | 9   | -             | -            | -            | -           | -            | -           | -            | -           | -2.60         | -2.60        | F             | -0.60         | *               |
| Leu | 10  | -             | -            | -            | -           | -            | -           | -            | -           | -2.60         | -2.60        | F             | -0.60         | *               |
| Leu | 11  | -             | -            | -            | -           | -            | -           | -            | -           | -2.60         | -2.60        | F             | -0.60         | *               |
| Pro | 12  | -             | -            | -            | -           | -            | -           | -            | -           | -2.60         | -2.60        | F             | -0.05         | 0.25            |
| Pro | 13  | -             | -            | -            | -           | -            | -           | -            | -           | -2.13         | -2.13        | F             | -0.05         | 0.25            |
| Leu | 14  | -             | -            | -            | -           | -            | -           | -            | -           | -1.91         | -1.91        | F             | -0.20         | 0.30            |
| Leu | 15  | -             | -            | -            | -           | -            | -           | -            | -           | -1.80         | -1.80        | F             | -0.20         | 0.20            |
| Leu | 16  | -             | -            | -            | -           | -            | -           | -            | -           | -1.20         | -1.20        | F             | -0.40         | 0.11            |
| Gly | 17  | -             | -            | -            | -           | -            | -           | -            | -           | -1.58         | -1.58        | F             | -0.40         | 0.39            |
| Ala | 18  | -             | -            | -            | -           | -            | -           | -            | -           | -1.36         | -1.36        | F             | -0.40         | 0.48            |
| Phe | 19  | -             | -            | -            | -           | -            | -           | -            | -           | -1.13         | -1.13        | F             | -0.40         | 0.49            |
| Pro | 20  | -             | -            | -            | -           | -            | -           | -            | -           | -0.91         | -0.91        | F             | -0.60         | 0.57            |
| Pro | 21  | -             | -            | -            | -           | -            | -           | -            | -           | -0.46         | -0.46        | F             | 0.30          | 0.72            |
| Ala | 22  | -             | -            | -            | -           | -            | -           | -            | -           | -0.21         | -0.21        | F             | 0.30          | 0.46            |
| Ala | 23  | -             | -            | -            | -           | -            | -           | -            | -           | 0.28          | 0.28         | F             | 0.70          | 0.71            |
| Ala | 24  | -             | -            | -            | -           | -            | -           | -            | -           | 0.28          | 0.28         | F             | 0.70          | *               |
| Ala | 25  | -             | -            | -            | -           | -            | -           | -            | -           | -             | -            | F             | -             | *               |

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| Res | Pos | Garni_Alpha | Chou_Alpha | Garni_Beta | Chou_Beta | Garni_Turn | Chou_Turn | Garni_Coil | Chou_Coil | Kyte_Hydro | Eisen_Alpho | Eisen_Beta | Karp_Flexi | Jones_Antiq | Emini_Surfact |
|-----|-----|-------------|------------|------------|-----------|------------|-----------|------------|-----------|------------|-------------|------------|------------|-------------|---------------|
| Arg | 26  | A           | A          | -          | -         | -          | -         | C          | C         | 0.53       | *           | *          | F          | 1.14        | 1.08          |
| Gly | 27  | -           | -          | -          | -         | -          | -         | C          | C         | 0.52       | *           | *          | F          | 1.78        | 2.15          |
| Pro | 28  | -           | -          | -          | -         | -          | -         | C          | C         | 0.52       | *           | *          | F          | 2.52        | 2.10          |
| Pro | 29  | -           | -          | -          | -         | -          | -         | C          | C         | 1.11       | *           | *          | F          | 2.06        | 1.08          |
| Lys | 30  | -           | -          | -          | -         | -          | -         | C          | C         | 1.74       | *           | *          | F          | 3.40        | 1.83          |
| Met | 31  | -           | -          | -          | -         | -          | -         | C          | C         | 0.78       | *           | *          | F          | 2.51        | 2.37          |
| Ala | 32  | -           | -          | -          | -         | -          | -         | C          | C         | 0.27       | *           | *          | F          | 1.77        | 1.14          |
| Asp | 33  | -           | -          | -          | -         | -          | -         | C          | C         | 0.27       | *           | *          | F          | 1.43        | 0.42          |
| Lys | 34  | -           | -          | -          | -         | -          | -         | C          | C         | 0.59       | *           | *          | F          | 0.79        | 0.66          |
| Val | 35  | -           | -          | -          | -         | -          | -         | C          | C         | 0.54       | *           | *          | F          | 0.90        | 1.28          |
| Val | 36  | -           | -          | -          | -         | -          | -         | C          | C         | 0.29       | *           | *          | F          | 0.90        | 1.32          |
| Pro | 37  | -           | -          | -          | -         | -          | -         | B          | B         | 0.29       | *           | *          | F          | 0.45        | 0.49          |
| Arg | 38  | -           | -          | -          | -         | -          | -         | B          | B         | 0.40       | *           | *          | F          | -0.15       | 0.67          |
| Gln | 39  | -           | -          | -          | -         | -          | -         | A          | A         | -0.46      | *           | *          | F          | 0.45        | 1.77          |
| Val | 40  | -           | -          | -          | -         | -          | -         | B          | B         | 0.06       | *           | *          | F          | 0.30        | 0.94          |
| Ala | 41  | -           | -          | -          | -         | -          | -         | A          | A         | 1.02       | *           | *          | F          | 0.30        | 0.48          |
| Arg | 42  | -           | -          | -          | -         | -          | -         | B          | B         | 0.92       | *           | *          | F          | 0.30        | 0.54          |
| Gly | 43  | -           | -          | -          | -         | -          | -         | B          | B         | -0.04      | *           | *          | F          | 0.45        | 1.05          |
| Arg | 44  | -           | -          | -          | -         | -          | -         | B          | B         | 0.07       | *           | *          | F          | 0.85        | 0.77          |
| Leu | 45  | -           | -          | -          | -         | -          | -         | B          | B         | 0.11       | *           | *          | F          | 0.75        | 0.77          |
| Gly | 46  | -           | -          | -          | -         | -          | -         | B          | B         | 0.70       | *           | *          | F          | 0.45        | 0.77          |
| Thr | 47  | -           | -          | -          | -         | -          | -         | B          | B         | -0.08      | *           | *          | F          | 0.45        | 1.55          |
| Val | 48  | -           | -          | -          | -         | -          | -         | B          | B         | 0.52       | *           | *          | F          | 0.30        | 0.37          |
| Arg | 49  | -           | -          | -          | -         | -          | -         | B          | B         | 0.01       | *           | *          | F          | -0.30       | 0.39          |
| Leu | 50  | -           | -          | -          | -         | -          | -         | B          | B         | -0.10      | *           | *          | F          | 0.00        | 0.39          |
| Gln |     |             |            |            |           |            |           |            |           |            |             |            |            |             |               |

FIG. 4B

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| Res | Pos | Garni-<br>Alpha | Chou-<br>Alpha | Garni-<br>Beta | Chou-<br>Beta | Garni-<br>Turn | Chou-<br>Turn | Kyte-<br>Garni-<br>Coil | Eisen-<br>Kyte-<br>Hydro- | Korpi-<br>Eisen-<br>Alpha | Korpi-<br>Eisen-<br>Beta | Jones-<br>Antig-<br>Flexi- | Emini-<br>Surfa- |
|-----|-----|-----------------|----------------|----------------|---------------|----------------|---------------|-------------------------|---------------------------|---------------------------|--------------------------|----------------------------|------------------|
| Cys | 51  |                 |                | B              | B             |                |               | -0.13                   | 0.72                      |                           |                          | 0.90                       | 0.35             |
| Pro | 52  |                 |                | B              | B             |                |               | 0.40                    | 1.00                      |                           |                          | 0.60                       | 0.42             |
| Val | 53  |                 |                |                |               | T              |               | 0.79                    | 0.64                      |                           |                          | 2.40                       | 0.40             |
| Glu | 54  |                 |                |                |               | I              |               | 0.79                    | 0.79                      |                           |                          | 3.00                       | 1.16             |
| Gly | 55  |                 |                |                |               | C              |               | 0.64                    | 0.64                      |                           |                          | 2.70                       | 1.16             |
| Asp | 56  |                 |                |                |               | C              |               | 0.54                    | 0.54                      |                           |                          | 2.40                       | 2.43             |
| Pro | 57  |                 |                |                |               | C              |               | 0.80                    | 0.51                      |                           |                          | 2.10                       | 1.16             |
| Pro | 58  |                 |                |                |               | C              |               | 0.54                    | 0.54                      |                           |                          | 1.50                       | 1.68             |
| Pro | 59  |                 |                |                |               | C              |               | 0.59                    | 0.59                      |                           |                          | 0.45                       | 1.00             |
| Leu | 60  |                 |                |                |               | B              |               | 0.80                    | *                         |                           |                          | -0.50                      | 0.66             |
| Thr | 61  |                 |                |                |               | B              |               | 0.67                    | *                         |                           |                          | -0.26                      | 0.63             |
| Met | 62  |                 |                |                |               | B              |               | 0.99                    | *                         |                           |                          | 0.87                       | 0.82             |
| Trp | 63  |                 |                |                |               | B              |               | 1.49                    | *                         |                           |                          | 2.36                       | 1.14             |
| Thr | 64  |                 |                |                |               | T              |               | 1.49                    | *                         |                           |                          | 3.40                       | 2.25             |
| Lys | 65  |                 |                |                |               | T              |               | 0.91                    | *                         |                           |                          | 3.06                       | 3.09             |
| Asp | 66  |                 |                |                |               | T              |               | 1.43                    | *                         |                           |                          | 2.72                       | 1.50             |
| Gly | 67  |                 |                |                |               | B              |               | 1.47                    | *                         |                           |                          | 1.58                       | 1.02             |
| Arg | 68  |                 |                |                |               | B              |               | 1.43                    | *                         |                           |                          | 1.09                       | 0.82             |
| Thr | 69  |                 |                |                |               | B              |               | 1.10                    | *                         |                           |                          | 0.30                       | 0.82             |
| Ile | 70  |                 |                |                |               | B              |               | 0.80                    | *                         |                           |                          | 0.30                       | 0.44             |
| His | 71  |                 |                |                |               | C              |               | 1.26                    | *                         |                           |                          | 0.00                       | 0.41             |
| Ser | 72  |                 |                |                |               | T              |               | 1.26                    | *                         |                           |                          | 0.87                       | 0.73             |
| Gly | 73  |                 |                |                |               | T              |               | 0.87                    | *                         |                           |                          | 0.65                       | 1.06             |
| Trp | 74  |                 |                |                |               | B              |               | 0.90                    | *                         |                           |                          |                            |                  |
| Ser | 75  |                 |                |                |               | C              |               |                         |                           |                           |                          |                            |                  |

FIG. 4C

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| Res | Pos | Gorni_Alpha | Chou_Alpha | Gorni_Beta | Chou_Beta | Gorni_Turn | Chou_Turn | Gorni_Coil | Chou_Coil | Kyte_Hydro | Eisen_Alpho | Eisen_Beta | Korpi_Flexi | James_Antig | Emini_Surf0 |
|-----|-----|-------------|------------|------------|-----------|------------|-----------|------------|-----------|------------|-------------|------------|-------------|-------------|-------------|
| Arg | 76  | B           | B          | B          | B         | T          | T         | C          | C         | 0.12       | *           | *          | -           | 0.10        | 0.80        |
| Phe | 77  | B           | B          | B          | B         | T          | T         | C          | C         | 0.21       | *           | *          | -0.60       | 0.62        |             |
| Arg | 78  | B           | B          | B          | B         | T          | T         | C          | C         | 0.56       | *           | *          | -0.30       | 0.72        |             |
| Val | 79  | B           | B          | B          | B         | T          | T         | C          | C         | 0.51       | *           | *          | -0.30       | 0.64        |             |
| Leu | 80  | B           | B          | B          | B         | T          | T         | C          | C         | -0.01      | *           | *          | -0.30       | 0.73        |             |
| Pro | 81  | B           | B          | B          | B         | T          | T         | C          | C         | -0.08      | *           | *          | -0.45       | 0.31        |             |
| Gln | 82  | A           | A          | A          | A         | T          | T         | C          | C         | -0.23      | *           | *          | -0.65       | 0.83        |             |
| Gly | 83  | A           | A          | A          | A         | T          | T         | C          | C         | 0.56       | *           | *          | -0.45       | 0.74        |             |
| Leu | 84  | A           | A          | A          | A         | T          | T         | C          | C         | 0.51       | *           | *          | -0.45       | 0.96        |             |
| Lys | 85  | A           | A          | A          | A         | T          | T         | C          | C         | 0.72       | *           | *          | -0.45       | 0.72        |             |
| Val | 86  | A           | A          | A          | A         | T          | T         | C          | C         | 0.83       | *           | *          | -0.90       | 1.51        |             |
| Lys | 87  | A           | A          | A          | A         | T          | T         | C          | C         | 1.18       | *           | *          | -0.90       | 1.48        |             |
| Gln | 88  | A           | A          | A          | A         | T          | T         | C          | C         | 1.99       | *           | *          | -0.90       | 3.46        |             |
| Val | 89  | A           | A          | A          | A         | T          | T         | C          | C         | 1.36       | *           | *          | -0.90       | 2.89        |             |
| Glu | 90  | A           | A          | B          | B         | T          | T         | T          | T         | 1.87       | *           | *          | -1.52       | 1.68        |             |
| Arg | 91  | A           | A          | B          | B         | T          | T         | T          | T         | 0.97       | *           | *          | -1.83       | 2.25        |             |
| Glu | 92  | A           | A          | B          | B         | T          | T         | T          | T         | 0.72       | *           | *          | -2.79       | 0.96        |             |
| Asp | 93  | B           | B          | B          | B         | T          | T         | T          | T         | 0.05       | *           | *          | -3.10       | 0.77        |             |
| Ala | 94  | B           | B          | B          | B         | T          | T         | T          | T         | -0.01      | *           | *          | -2.34       | 0.33        |             |
| Cly | 95  | B           | B          | B          | B         | T          | T         | T          | T         | -0.60      | *           | *          | -0.73       | 0.11        |             |
| Val | 96  | B           | B          | B          | B         | T          | T         | T          | T         | -0.91      | *           | *          | -0.02       | 0.21        |             |
| Tyr | 97  | B           | B          | B          | B         | T          | T         | T          | T         | -0.32      | *           | *          | -0.29       | 0.21        |             |
| Val | 98  | B           | B          | B          | B         | T          | T         | T          | T         | -0.32      | *           | *          | -0.60       | 0.42        |             |
| Cys | 99  | B           | B          | B          | B         | T          | T         | T          | T         | -0.32      | *           | *          | -0.30       | 0.43        |             |
| Lys | 100 | B           | B          | B          | B         | T          | T         | T          | T         | -0.32      | *           | *          | -0.30       | 0.43        |             |

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FIG. 4D

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| Res | Pos | Garni-Alpha | Chou-Alpha | Garni-Beta | Chou-Beta | Garni-Turn | Chou-Turn | Garni-Coil | Chou-Coil | Kyte-Hydro | Eisen-Alpha | Eisen-Beta | Karp-Flexi | Jones-Antig. | Emini-Surfα |
|-----|-----|-------------|------------|------------|-----------|------------|-----------|------------|-----------|------------|-------------|------------|------------|--------------|-------------|
| Ala | 101 | B           | B          | B          | B         | T          | T         | -0.17      | *         | F          | F           | F          | F          | 0.57         |             |
| Thr | 102 | -           | -          | -          | -         | -          | -         | -0.27      | *         | F          | F           | F          | F          | 0.92         |             |
| Asn | 103 | -           | -          | -          | -         | -          | -         | 0.29       | *         | F          | F           | F          | F          | 0.46         |             |
| Gly | 104 | -           | -          | -          | -         | -          | -         | 0.14       | *         | F          | F           | F          | F          | 0.60         |             |
| Phe | 105 | -           | -          | -          | -         | -          | -         | -0.20      | *         | F          | F           | F          | F          | 0.35         |             |
| Gly | 106 | -           | -          | -          | -         | -          | -         | -0.47      | *         | F          | F           | F          | F          | 0.29         |             |
| Ser | 107 | -           | -          | -          | -         | -          | -         | -0.16      | *         | F          | F           | F          | F          | 0.22         |             |
| Leu | 108 | B           | B          | B          | B         | B          | B         | -0.40      | *         | F          | F           | F          | F          | 0.40         |             |
| Ser | 109 | B           | B          | B          | B         | B          | B         | -0.37      | *         | F          | F           | F          | F          | 0.40         |             |
| Val | 110 | B           | B          | B          | B         | B          | B         | -0.48      | *         | F          | F           | F          | F          | 0.40         |             |
| Asn | 111 | B           | B          | B          | B         | B          | B         | -0.99      | *         | F          | F           | F          | F          | 0.63         |             |
| Tyr | 112 | B           | B          | B          | B         | B          | B         | -1.54      | *         | F          | F           | F          | F          | 0.68         |             |
| Thr | 113 | B           | B          | B          | B         | B          | B         | -1.54      | *         | F          | F           | F          | F          | 0.38         |             |
| Leu | 114 | B           | B          | B          | B         | B          | B         | -1.24      | *         | F          | F           | F          | F          | 0.60         |             |
| Val | 115 | B           | B          | B          | B         | B          | B         | -0.39      | *         | F          | F           | F          | F          | 0.19         |             |
| Val | 116 | B           | B          | B          | B         | B          | B         | -1.28      | *         | F          | F           | F          | F          | 0.38         |             |
| Leu | 117 | B           | B          | B          | B         | B          | B         | -1.33      | *         | F          | F           | F          | F          | 0.60         |             |
| Asp | 118 | B           | B          | B          | B         | B          | B         | -1.23      | *         | F          | F           | F          | F          | 0.21         |             |
| Asp | 119 | B           | B          | B          | B         | B          | B         | -0.77      | *         | F          | F           | F          | F          | 0.37         |             |
| Ile | 120 | B           | B          | B          | B         | B          | B         | 0.13       | *         | F          | F           | F          | F          | 0.77         |             |
| Ser | 121 | B           | B          | B          | B         | B          | B         | 0.99       | *         | F          | F           | F          | F          | 1.14         |             |
| Pro | 122 | B           | B          | B          | B         | B          | B         | 1.50       | *         | F          | F           | F          | F          | 0.92         |             |
| Gly | 123 | B           | B          | B          | B         | B          | B         | 0.69       | *         | F          | F           | F          | F          | 2.52         |             |
| Lys | 124 | B           | B          | B          | B         | B          | B         | 0.34       | *         | F          | F           | F          | F          | 1.16         |             |
| Glu | 125 | B           | B          | B          | B         | B          | B         | 1.02       | *         | F          | F           | F          | F          | 2.86         |             |

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| Res | Pos | Gorni_Alpha | Chou_Alpha | Gorni_Beta | Chou_Beta | Gorni_Turn | Chou_Turn | Gorni_Coil | Chou_Coil | Kyle_Hyde | Eisen_Alpho | Eisen_Beta | Korpl_Flex | James_Antig | Emini_Surfa |
|-----|-----|-------------|------------|------------|-----------|------------|-----------|------------|-----------|-----------|-------------|------------|------------|-------------|-------------|
| Ser | 126 | -           | -          | B          | B         | -          | -         | -          | -         | 1.32      | -           | -          | F          | 1.28        | 1.34        |
| Ile | 127 | -           | -          | B          | B         | -          | -         | -          | -         | 1.23      | -           | -          | F          | 1.74        | 1.12        |
| Cy  | 128 | -           | -          | B          | B         | -          | -         | -          | -         | 0.93      | -           | -          | F          | 1.75        | 0.87        |
| Pro | 129 | -           | -          | -          | -         | -          | -         | -          | -         | 0.59      | -           | -          | F          | 2.60        | 1.41        |
| Asp | 130 | -           | -          | -          | -         | -          | -         | -          | -         | 0.54      | -           | -          | F          | 3.00        | 1.41        |
| Ser | 131 | -           | -          | -          | -         | -          | -         | -          | -         | 1.36      | -           | -          | F          | 2.55        | 0.90        |
| Ser | 132 | -           | -          | -          | -         | -          | -         | -          | -         | 1.70      | -           | -          | F          | 2.25        | 0.94        |
| Ser | 133 | -           | -          | -          | -         | -          | -         | -          | -         | 1.91      | -           | -          | F          | 2.10        | 1.21        |
| Cly | 134 | -           | -          | -          | -         | -          | -         | -          | -         | 1.70      | -           | -          | F          | 1.80        | 1.51        |
| Cly | 135 | -           | -          | -          | -         | -          | -         | -          | -         | 1.41      | -           | -          | F          | 1.64        | 1.74        |
| Cln | 136 | -           | -          | -          | -         | -          | -         | -          | -         | 1.41      | -           | -          | F          | 1.98        | 1.77        |
| GLU | 137 | -           | -          | -          | -         | -          | -         | -          | -         | 1.71      | -           | -          | F          | 2.52        | 2.40        |
| Asp | 138 | -           | -          | -          | -         | -          | -         | -          | -         | 2.05      | -           | -          | F          | 2.86        | 2.40        |
| Pro | 139 | -           | -          | -          | -         | -          | -         | -          | -         | 2.11      | -           | -          | F          | 3.49        | 2.40        |
| Alo | 140 | -           | -          | -          | -         | -          | -         | -          | -         | 1.52      | -           | -          | F          | 1.96        | 1.51        |
| Ser | 141 | -           | -          | -          | -         | -          | -         | -          | -         | 1.63      | -           | -          | F          | 0.77        | 0.99        |
| Cln | 142 | -           | -          | -          | -         | -          | -         | -          | -         | 1.42      | -           | -          | F          | 1.28        | 1.92        |
| Trp | 143 | -           | -          | -          | -         | -          | -         | -          | -         | 1.74      | -           | -          | F          | 0.94        | 2.21        |
| Alo | 145 | -           | -          | -          | -         | -          | -         | -          | -         | 1.63      | -           | -          | F          | 0.65        | 2.50        |
| Arg | 146 | -           | -          | -          | -         | -          | -         | -          | -         | 1.62      | -           | -          | F          | 0.25        | 1.25        |
| Pro | 147 | -           | -          | -          | -         | -          | -         | -          | -         | 1.62      | -           | -          | F          | 0.40        | 1.72        |
| Arg | 148 | -           | -          | -          | -         | -          | -         | -          | -         | 1.41      | -           | -          | F          | 1.40        | 2.94        |
| Phe | 149 | -           | -          | -          | -         | -          | -         | -          | -         | 1.40      | -           | -          | F          | 1.74        | 2.52        |
| Thr | 150 | -           | -          | -          | -         | -          | -         | -          | -         | 2.03      | -           | -          | F          | 1.68        | 2.01        |

FIG. 4F

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| Res | Pos | Garni_Alpho | Ghouv_Alpho | Garni_Beta | Chou_Beta | Garni_Turn | Chou_Turn | Garni_Coil | Chou_Coil | Kyte_Hydro | Eisen_Alpha | Eisen_Beta | Korpi_Flexi | Jones_Antig | Emini_Surfa |
|-----|-----|-------------|-------------|------------|-----------|------------|-----------|------------|-----------|------------|-------------|------------|-------------|-------------|-------------|
| Gln | 151 | -           | -           | -          | -         | T          | C         | 1.32       | -         | F          | *           | *          | F           | 2.52        | 2.06        |
| Pro | 152 | -           | -           | -          | -         | T          | C         | 1.64       | -         | F          | *           | *          | F           | 1.96        | 2.35        |
| Ser | 153 | -           | -           | -          | -         | T          | C         | 2.46       | -         | F          | *           | *          | F           | 3.40        | 3.19        |
| Lys | 154 | -           | -           | -          | -         | T          | C         | 1.91       | -         | F          | *           | *          | F           | 3.06        | 3.61        |
| Met | 155 | -           | -           | -          | -         | B          | B         | 1.02       | -         | F          | *           | *          | F           | 2.12        | 4.57        |
| Arg | 156 | -           | -           | -          | -         | B          | B         | 0.64       | -         | F          | *           | *          | F           | 1.58        | 2.53        |
| Arg | 157 | -           | -           | -          | -         | B          | B         | 1.05       | -         | F          | *           | *          | F           | 1.09        | 0.89        |
| Val | 158 | -           | -           | -          | -         | B          | B         | 0.80       | -         | F          | *           | *          | F           | 0.60        | 0.91        |
| Ile | 159 | -           | -           | -          | -         | B          | B         | 0.54       | -         | F          | *           | *          | F           | 0.60        | 0.71        |
| Ala | 160 | -           | -           | -          | -         | B          | B         | 0.09       | -         | F          | *           | *          | F           | 0.55        | 0.27        |
| Arg | 161 | -           | -           | -          | -         | B          | B         | 0.32       | -         | F          | *           | *          | F           | 0.20        | 0.36        |
| Arg | 162 | -           | -           | -          | -         | B          | B         | 0.73       | -         | F          | *           | *          | F           | 1.00        | 0.69        |
| Pro | 163 | -           | -           | -          | -         | B          | B         | 0.73       | -         | F          | *           | *          | F           | 2.50        | 0.35        |
| Val | 164 | -           | -           | -          | -         | B          | B         | 0.27       | -         | F          | *           | *          | F           | 2.25        | 0.92        |
| Gly | 165 | -           | -           | -          | -         | B          | B         | 0.04       | -         | F          | *           | *          | F           | 1.85        | 0.44        |
| Ser | 166 | -           | -           | -          | -         | B          | B         | -0.02      | -         | F          | *           | *          | F           | 0.60        | 0.49        |
| Ser | 167 | -           | -           | -          | -         | B          | B         | -0.48      | -         | F          | *           | *          | F           | 0.95        | 0.99        |
| Val | 168 | -           | -           | -          | -         | B          | B         | -0.48      | -         | F          | *           | *          | F           | 0.55        | 0.39        |
| Arg | 169 | -           | -           | -          | -         | B          | B         | -0.72      | -         | F          | *           | *          | F           | 0.30        | 0.22        |
| Leu | 170 | -           | -           | -          | -         | B          | B         | -0.72      | -         | F          | *           | *          | F           | -0.30       | 0.30        |
| Lys | 171 | -           | -           | -          | -         | B          | B         | -0.77      | -         | F          | *           | *          | F           | 0.30        | 0.20        |
| Cys | 172 | -           | -           | -          | -         | B          | B         | -0.06      | -         | F          | *           | *          | F           | -0.30       | 0.24        |
| Val | 173 | -           | -           | -          | -         | B          | B         | -0.27      | -         | F          | *           | *          | F           | 0.00        | 0.17        |
| Ala | 174 | -           | -           | -          | -         | B          | B         | -0.66      | -         | F          | *           | *          | F           | 0.00        | 0.48        |
| Ser | 175 | -           | -           | -          | -         | B          | B         | -0.66      | -         | F          | *           | *          | F           | 0.00        | 0.48        |

FIG. 4G

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| Res | Pos | Garni - Alpha | Garni - Alpha | Garni - Beta | Garni - Beta | Chau - Turn | Chau - Turn | Gorni - Coil | Gorni - Coil | Kyle - Hydra | Eisen - Alpha | Eisen - Beta | Karpf - Flexi | Jones - Antig | Emini - Surfo |
|-----|-----|---------------|---------------|--------------|--------------|-------------|-------------|--------------|--------------|--------------|---------------|--------------|---------------|---------------|---------------|
| Gly | 176 |               |               |              |              |             |             | C            | C            | 0.40         | *             | *            | F             | 1.90          | 1.27          |
| His | 177 |               |               |              |              |             |             | C            | C            | 1.07         | *             | *            | F             | 2.40          | 1.94          |
| Pro | 178 |               |               |              |              |             |             | C            | C            | 1.03         | *             | *            | F             | 3.00          | 2.41          |
| Arg | 179 |               |               |              |              |             |             | C            | C            | 1.31         | *             | *            | F             | 2.70          | 1.71          |
| Pro | 180 |               |               |              |              |             |             | C            | C            | 1.32         | *             | *            | F             | 2.30          | 1.81          |
| Asp | 181 |               |               |              |              |             |             | C            | C            | 1.07         | *             | *            | F             | 1.80          | 1.23          |
| Ile | 182 |               |               |              |              |             |             | C            | C            | 1.14         | *             | *            | F             | 0.00          | 0.62          |
| Thr | 183 |               |               |              |              |             |             | C            | C            | 1.36         | *             | *            | F             | 0.04          | 0.81          |
| Asp | 184 |               |               |              |              |             |             | C            | C            | 1.24         | *             | *            | F             | 0.98          | 0.81          |
| Trp | 185 |               |               |              |              |             |             | C            | C            | 1.46         | *             | *            | F             | 1.47          | 1.92          |
| Met | 186 |               |               |              |              |             |             | C            | C            | 0.87         | *             | *            | F             | 2.51          | 2.30          |
| Lys | 187 |               |               |              |              |             |             | C            | C            | 0.94         | *             | *            | F             | 3.40          | 2.21          |
| Asp | 188 |               |               |              |              |             |             | C            | C            | 0.94         | *             | *            | F             | 3.06          | 1.84          |
| Gln | 189 |               |               |              |              |             |             | C            | C            | 1.34         | *             | *            | F             | 2.52          | 1.33          |
| Ala | 190 |               |               |              |              |             |             | C            | C            | 1.73         | *             | *            | F             | 1.63          | 1.56          |
| Leu | 191 |               |               |              |              |             |             | C            | C            | 1.69         | *             | *            | F             | 1.14          | 1.45          |
| Thr | 192 |               |               |              |              |             |             | C            | C            | 1.10         | *             | *            | F             | 0.80          | 1.45          |
| Arg | 193 |               |               |              |              |             |             | C            | C            | 0.51         | *             | *            | F             | 0.80          | 1.77          |
| Pro | 194 |               |               |              |              |             |             | C            | C            | 0.51         | *             | *            | F             | 0.90          | 2.13          |
| Glu | 195 |               |               |              |              |             |             | C            | C            | 0.88         | *             | *            | F             | 0.90          | 1.68          |
| Ala | 196 |               |               |              |              |             |             | C            | C            | 1.81         | *             | *            | F             | 0.90          | 2.13          |
| Ala | 197 |               |               |              |              |             |             | C            | C            | 2.17         | *             | *            | F             | 0.90          | 2.45          |
| Glu | 198 |               |               |              |              |             |             | C            | C            | 2.10         | *             | *            | F             | 0.90          | 4.86          |
| Pro | 199 |               |               |              |              |             |             | C            | C            | 2.35         | *             | *            | F             | 2.07          | 9.62          |
| Arg | 200 |               |               |              |              |             |             | C            | C            | 2.07         | *             | *            | F             | 1.30          |               |

SUBSTITUTE SHEET (RULE 26)

FIG. 4H

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| Res | Pos | Garni-<br>Alpha | Chou-<br>Alpha | Garni-<br>Beta | Chou-<br>Beta | Garni-<br>Turn | Chou-<br>Turn | Garni-<br>Coil | Kyte-<br>Hydro | Eisen-<br>Alpha | Eisen-<br>Beta | Korpi-<br>Flexi | James-<br>Antig | Emini-<br>Surf0- |
|-----|-----|-----------------|----------------|----------------|---------------|----------------|---------------|----------------|----------------|-----------------|----------------|-----------------|-----------------|------------------|
| Lys | 201 | A               | A              | A              | B             | B              | B             | C              | 2.34           | -               | F              | 0.90            | 5.84            |                  |
| Lys | 202 | -               | -              | A              | A             | A              | A             | C              | 2.12           | -               | F              | 1.30            | 5.45            |                  |
| Lys | 203 | -               | -              | A              | A             | A              | A             | C              | 1.82           | -               | F              | 1.30            | 2.29            |                  |
| Trp | 204 | -               | -              | A              | A             | A              | A             | C              | 1.22           | -               | *              | 0.75            | 1.54            |                  |
| Thr | 205 | -               | -              | A              | A             | A              | A             | C              | 1.16           | -               | *              | -0.39           | 0.63            |                  |
| Leu | 206 | -               | -              | A              | A             | A              | A             | C              | 0.26           | +               | *              | -0.39           | 0.63            |                  |
| Ser | 207 | -               | -              | A              | A             | A              | A             | C              | 0.32           | +               | *              | -0.60           | 0.97            |                  |
| Leu | 208 | -               | -              | A              | A             | A              | A             | C              | 0.40           | +               | *              | -0.30           | 0.55            |                  |
| Lys | 209 | -               | -              | A              | A             | A              | A             | C              | 0.71           | +               | F              | 1.00            | 1.32            |                  |
| Asn | 210 | -               | -              | A              | A             | A              | A             | C              | 1.52           | +               | F              | 0.80            | 1.52            |                  |
| Leu | 211 | -               | -              | A              | A             | A              | A             | C              | 1.52           | +               | F              | 1.44            | 3.19            |                  |
| Arg | 212 | -               | -              | A              | A             | A              | A             | C              | 1.99           | +               | F              | 1.58            | 2.66            |                  |
| Pro | 213 | -               | -              | A              | A             | A              | A             | C              | 1.99           | +               | F              | 2.12            | 2.22            |                  |
| Glu | 214 | -               | -              | A              | A             | A              | A             | C              | 1.74           | +               | F              | 2.86            | 2.66            |                  |
| Asp | 215 | -               | -              | A              | A             | A              | A             | C              | 2.24           | +               | F              | 3.40            | 2.76            |                  |
| Ser | 216 | -               | -              | A              | A             | A              | A             | C              | 1.47           | +               | F              | 2.72            | 2.30            |                  |
| Gly | 217 | -               | -              | A              | A             | A              | A             | C              | 1.79           | +               | F              | 1.93            | 0.74            |                  |
| Lys | 218 | -               | -              | A              | A             | A              | A             | C              | 0.93           | +               | F              | 0.94            | 1.08            |                  |
| Tyr | 219 | -               | -              | A              | A             | A              | A             | C              | 0.63           | +               | F              | 0.56            | 0.81            |                  |
| Thr | 220 | -               | -              | A              | A             | A              | A             | C              | 0.93           | +               | F              | 0.82            | 0.54            |                  |
| Cys | 221 | -               | -              | A              | A             | A              | A             | C              | 1.39           | +               | F              | 0.48            | 0.56            |                  |
| Arg | 222 | -               | -              | A              | A             | A              | A             | C              | 0.76           | +               | F              | 2.04            | 0.75            |                  |
| Val | 223 | -               | -              | A              | A             | A              | A             | C              | 0.66           | +               | F              | 2.60            | 1.42            |                  |
| Ser | 224 | -               | -              | A              | A             | A              | A             | C              | 0.36           | +               | F              | 2.19            | 0.72            |                  |
| Asn | 225 | -               | -              | A              | A             | A              | A             | C              | 0.16           | +               | F              | 2.03            | 0.88            |                  |
| Arg | 226 | -               | -              | -              | -             | -              | -             | -              | -              | -               | -              | -               | -               | -                |

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| Res | Pos | Gorni_Alpho | Chou_Alpho | Gorni_Beta | Chou_Beta | Gorni_Turn | Chou_Turn | Garni_Coil | Kyle_Hydro | Eisen_Alpha | Eisen_Beta | Karpf_Flexi | James_Antiq | Emini_Surfa |
|-----|-----|-------------|------------|------------|-----------|------------|-----------|------------|------------|-------------|------------|-------------|-------------|-------------|
| Ala | 227 | -           | -          | -          | -         | T          | -         | C          | 0.04       | *           | *          | F           | 1.57        | 0.51        |
| Gly | 228 | -           | -          | B          | B         | -          | -         | C          | 0.31       | -           | -          | 0.96        | 0.51        |             |
| Ala | 229 | -           | -          | B          | B         | -          | -         | C          | 0.30       | -           | -          | -0.10       | 0.26        |             |
| Ile | 230 | -           | -          | B          | B         | -          | -         | C          | 0.06       | -           | -          | -0.40       | 0.38        |             |
| Asn | 231 | -           | -          | B          | B         | -          | -         | C          | -0.01      | -           | -          | -0.20       | 0.60        |             |
| Ala | 232 | -           | -          | B          | B         | -          | -         | C          | -0.28      | -           | -          | 0.25        | 1.18        |             |
| Ile | 233 | -           | -          | B          | B         | -          | -         | C          | 0.07       | -           | -          | -0.05       | 1.25        |             |
| Tyr | 234 | -           | -          | B          | B         | -          | -         | C          | -0.20      | -           | -          | 0.85        | 1.30        |             |
| Lys | 235 | -           | -          | B          | B         | -          | -         | C          | -0.20      | -           | -          | -0.30       | 0.95        |             |
| Val | 236 | -           | -          | B          | B         | -          | -         | C          | -0.20      | -           | -          | -0.30       | 0.46        |             |
| Asp | 237 | -           | -          | B          | B         | -          | -         | C          | 0.50       | -           | -          | -0.30       | 0.51        |             |
| Val | 238 | -           | -          | B          | B         | -          | -         | C          | 0.50       | -           | -          | 0.60        | 0.50        |             |
| Ile | 239 | -           | -          | B          | B         | -          | -         | C          | 0.86       | -           | -          | 0.64        | 0.98        |             |
| Cln | 240 | -           | -          | B          | B         | -          | -         | C          | 0.51       | -           | -          | 1.43        | 1.14        |             |
| Arg | 241 | -           | -          | B          | B         | -          | -         | C          | 1.41       | -           | -          | 1.62        | 2.06        |             |
| Thr | 242 | -           | -          | B          | B         | -          | -         | C          | 1.20       | -           | -          | 3.06        | 5.89        |             |
| Arg | 243 | -           | -          | B          | B         | -          | -         | C          | 1.20       | -           | -          | 3.40        | 5.26        |             |
| Ser | 244 | -           | -          | B          | B         | -          | -         | C          | 1.28       | -           | -          | 2.86        | 1.99        |             |
| Lys | 245 | -           | -          | B          | B         | -          | -         | C          | 0.97       | -           | -          | 2.22        | 1.14        |             |
| Pro | 246 | -           | -          | B          | B         | -          | -         | C          | 0.51       | -           | -          | 1.13        | 0.84        |             |
| Val | 247 | -           | -          | B          | B         | -          | -         | C          | 0.51       | -           | -          | 0.19        | 0.62        |             |
| Leu | 248 | -           | -          | B          | B         | -          | -         | C          | 0.37       | -           | -          | -0.15       | 0.45        |             |
| Ile | 249 | -           | -          | B          | B         | -          | -         | C          | 0.46       | -           | -          | -0.45       | 0.39        |             |
| Gly | 250 | -           | -          | B          | B         | -          | -         | C          | -0.44      | -           | -          | -0.45       | 0.82        |             |
| Thr | 251 | -           | -          | B          | B         | -          | -         | C          | -0.23      | -           | -          | -0.45       | 0.74        |             |

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| Res | Pos | Garni-Alpha | Chou-Alpha | Garni-Beta | Chou-Beta | Garni-Turn | Chou-Turn | Garni-Coil | Chou-Coil | Kyte-Hydro | Eisen-Alpha | Karpf-Flexi | James-Antig. | Emini-Surf |
|-----|-----|-------------|------------|------------|-----------|------------|-----------|------------|-----------|------------|-------------|-------------|--------------|------------|
| His | 252 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.82       |
| Pro | 253 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 1.20       |
| Val | 254 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 1.20       |
| Asn | 255 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.65       |
| Thr | 256 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.71       |
| Thr | 257 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.71       |
| Val | 258 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.82       |
| Asp | 259 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.51       |
| Phe | 260 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.51       |
| Gly | 261 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.35       |
| Gly | 262 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.35       |
| Thr | 263 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.54       |
| Thr | 264 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.54       |
| Ser | 265 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.68       |
| Phe | 266 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.68       |
| Gln | 267 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.25       |
| Cys | 268 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 1.20       |
| Lys | 269 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.51       |
| Val | 270 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.35       |
| Arg | 271 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 2.15       |
| Ser | 272 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 2.31       |
| Asp | 273 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.97       |
| Val | 274 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.46       |
| Lys | 275 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.45       |
| Pro | 276 | -           | -          | -          | -         | -          | -         | -          | -         | -          | -           | -           | -            | 0.47       |

FIG. 4K

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| Res | Pos | Garni_Alpha | Chou_Alpha | Garni_Beta | Chou_Beta | Garni_Turn | Chou_Turn | Garni_Goil | Chou_Goil | Kyte_Hydro | Eisen_Alpha | Eisen_Beta | Karpl_Flexi | Jones_Antig | Emini_Surf0 |
|-----|-----|-------------|------------|------------|-----------|------------|-----------|------------|-----------|------------|-------------|------------|-------------|-------------|-------------|
| Val | 277 |             |            | B          | B         |            |           | -0.37      | *         | *          | *           | *          |             | -0.60       | 0.67        |
| Ile | 278 |             |            | B          | B         |            |           | -0.32      | *         | *          | *           | *          |             | -0.60       | 0.28        |
| Gln | 279 |             |            | B          | B         |            |           | 0.64       | *         | *          | *           | *          |             | -0.60       | 0.36        |
| Trp | 280 |             |            | B          | B         |            |           | -0.26      | *         | *          | *           | *          |             | -0.30       | 0.95        |
| Leu | 281 |             |            | B          | B         |            |           | -0.04      | *         | *          | *           | *          |             | -0.15       | 1.00        |
| Lys | 282 |             |            | B          | B         |            |           | 0.57       | *         | *          | *           | *          |             | 0.45        | 1.00        |
| Arg | 283 |             |            | B          | B         |            |           | 1.11       | *         | *          | *           | *          |             | 0.45        | 1.49        |
| Val | 284 |             |            | B          | B         |            |           | 0.52       | *         | *          | *           | *          |             | 0.45        | 1.79        |
| Glu | 285 |             |            | B          | B         |            |           | 0.81       | *         | *          | *           | *          |             | 0.60        | 0.90        |
| Tyr | 286 |             |            |            |           |            |           | 1.34       | *         | *          | *           | *          |             | 1.54        | 0.80        |
| Gly | 287 |             |            |            |           |            |           | 1.28       | *         | *          | *           | *          |             | 1.73        | 1.07        |
| Ala | 288 |             |            |            |           |            |           | 1.20       | *         | *          | *           | *          |             | 2.52        | 1.21        |
| Glu | 289 |             |            |            |           |            |           | 2.06       | *         | *          | *           | *          |             | 3.40        | 1.05        |
| Gly | 290 |             |            |            |           |            |           | 1.76       | *         | *          | *           | *          |             | 3.40        | 1.70        |
| Arg | 291 |             |            |            |           |            |           | 1.69       | *         | *          | *           | *          |             | 2.86        | 2.26        |
| His | 292 |             |            |            |           |            |           | 1.14       | *         | *          | *           | *          |             | 2.52        | 1.88        |
| Asn | 293 |             |            |            |           |            |           | 1.73       | *         | *          | *           | *          |             | 1.88        | 1.33        |
| Ser | 294 |             |            |            |           |            |           | 0.88       | *         | *          | *           | *          |             | 1.64        | 1.14        |
| Ile | 295 |             |            |            |           |            |           | 0.42       | *         | *          | *           | *          |             | 0.25        | 0.62        |
| Asp | 296 |             |            |            |           |            |           | 0.46       | *         | *          | *           | *          |             | 0.75        | 0.28        |
| Val | 297 |             |            |            |           |            |           | 0.50       | *         | *          | *           | *          |             | 1.00        | 0.34        |
| Gly | 298 |             |            |            |           |            |           | 0.10       | *         | *          | *           | *          |             | 2.25        | 0.96        |
| Gly | 299 |             |            |            |           |            |           | -0.44      | *         | *          | *           | *          |             | 2.50        | 0.50        |
| Gln | 300 |             |            |            |           |            |           | -0.51      | *         | *          | *           | *          |             | 0.85        | 0.50        |
|     | 301 |             |            |            |           |            |           |            |           |            |             |            |             |             |             |

SUBSTITUTE SHEET (RULE 26)

FIG. 4L

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| Res | Pos | Garni_Alpha | Chou_Alpha | Garni_Beta | Chou_Beta | Garni_Turn | Chou_Turn | Garni_Coil | Chou_Coil | Kyte_Hydro | Eisen_Alpha | Eisen_Beta | Karp_Flexi | Karp_Flexi | James_Artifg | Emini_Surfa |
|-----|-----|-------------|------------|------------|-----------|------------|-----------|------------|-----------|------------|-------------|------------|------------|------------|--------------|-------------|
| Lys | 302 | B           | B          | B          | B         | B          | B         | B          | B         | -1.22      | -0.58       | -0.54      | F          | F          | 0.60         | 0.37        |
| Phe | 303 | B           | B          | B          | B         | B          | B         | B          | B         | -0.58      | -0.54       | -0.54      | F          | F          | -0.10        | 0.31        |
| Val | 304 | B           | B          | B          | B         | B          | B         | B          | B         | -0.54      | -0.54       | -0.54      | F          | F          | -0.35        | 0.28        |
| Val | 305 | B           | B          | B          | B         | B          | B         | B          | B         | -0.54      | -0.54       | -0.54      | F          | F          | -0.60        | 0.20        |
| Leu | 306 | B           | B          | B          | B         | B          | B         | B          | B         | -0.54      | -0.54       | -0.54      | F          | F          | -0.20        | 0.23        |
| Pro | 307 | B           | B          | B          | B         | B          | B         | B          | B         | -1.44      | -1.03       | -0.48      | F          | F          | 0.25         | 0.52        |
| Thr | 308 | B           | B          | B          | B         | B          | B         | B          | B         | -0.48      | -0.48       | -0.48      | F          | F          | 0.65         | 0.52        |
| Gly | 309 | B           | B          | B          | B         | B          | B         | B          | B         | 0.49       | 0.49        | 0.49       | F          | F          | 0.35         | 0.66        |
| Asp | 310 | B           | B          | B          | B         | B          | B         | B          | B         | 1.09       | 1.09        | 1.09       | F          | F          | 0.25         | 0.57        |
| Val | 311 | B           | B          | B          | B         | B          | B         | B          | B         | 1.30       | 1.30        | 1.30       | F          | F          | 0.45         | 0.78        |
| Trp | 312 | B           | B          | B          | B         | B          | B         | B          | B         | 1.27       | 1.27        | 1.27       | F          | F          | 1.58         | 1.21        |
| Ser | 313 | B           | B          | B          | B         | B          | B         | B          | B         | 1.31       | 1.31        | 1.31       | F          | F          | 2.02         | 1.62        |
| Arg | 314 | B           | B          | B          | B         | B          | B         | B          | B         | 1.07       | 1.07        | 1.07       | F          | F          | 2.76         | 2.06        |
| Pro | 315 | B           | B          | B          | B         | B          | B         | B          | B         | 1.11       | 1.11        | 1.11       | F          | F          | 3.40         | 2.41        |
| Asp | 316 | B           | B          | B          | B         | B          | B         | B          | B         | 1.40       | 1.40        | 1.40       | F          | F          | 2.76         | 1.01        |
| Gly | 317 | B           | B          | B          | B         | B          | B         | B          | B         | 1.74       | 1.74        | 1.74       | F          | F          | 1.62         | 1.06        |
| Ser | 318 | B           | B          | B          | B         | B          | B         | B          | B         | 0.82       | 0.82        | 0.82       | F          | F          | 1.48         | 1.26        |
| Tyr | 319 | B           | B          | B          | B         | B          | B         | B          | B         | 0.22       | 0.22        | 0.22       | F          | F          | 0.54         | 1.05        |
| Leu | 320 | B           | B          | B          | B         | B          | B         | B          | B         | -0.67      | -0.67       | -0.67      | F          | F          | -0.40        | 0.65        |
| Asn | 321 | B           | B          | B          | B         | B          | B         | B          | B         | -0.63      | -0.63       | -0.63      | F          | F          | -0.60        | 0.29        |
| Lys | 322 | B           | B          | B          | B         | B          | B         | B          | B         | -0.22      | -0.22       | -0.22      | F          | F          | -0.68        | 0.51        |
| Leu | 323 | B           | B          | B          | B         | B          | B         | B          | B         | -0.57      | -0.57       | -0.57      | F          | F          | 0.30         | 0.52        |
| Ile | 324 | B           | B          | B          | B         | B          | B         | B          | B         | 0.36       | 0.36        | 0.36       | F          | F          | -0.30        | 0.31        |
| Ile | 325 | B           | B          | B          | B         | B          | B         | B          | B         | 0.36       | 0.36        | 0.36       | F          | F          | 0.04         | 0.74        |
|     | 326 |             |            |            |           |            |           |            |           |            |             |            |            |            |              |             |

FIG. 4M

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| Res | Pos | Gorri_ Alpha | Chou_ Alpha | Gorri_ Beta | Chou_ Beta | Gorri_ Turn | Chou_ Turn | Gorni_ Coil | Kyle_ Hydro | Eisen_ Alpha | Eisen_ Beta | Korpi_ Flexi | Jones_ Antig | Emini_ Surfo |
|-----|-----|--------------|-------------|-------------|------------|-------------|------------|-------------|-------------|--------------|-------------|--------------|--------------|--------------|
| Arg | 327 | B            | B           | B           | B          | I           | I          | *           | F           | 1.28         | 1.56        |              |              |              |
| Ala | 328 |              |             | B           | B          | I           | I          | *           | F           | 1.92         | 3.71        |              |              |              |
| Arg | 329 |              |             | B           |            | I           | I          | *           | F           | 2.66         | 4.29        |              |              |              |
| Cys | 330 |              |             |             |            | I           | I          |             | F           | 3.40         | 2.21        |              |              |              |
| Asp | 331 |              |             |             |            | I           | I          |             |             | 3.06         | 2.17        |              |              |              |
| Asp | 332 |              |             |             |            | I           | I          |             |             |              | 2.72        | 1.10         |              |              |
| Ala | 333 |              |             |             |            | I           | I          |             |             |              |             | 1.58         | 0.99         |              |
| Gly | 334 |              |             |             |            | I           | I          |             |             |              |             | 0.64         | 0.42         |              |
| Met | 335 |              |             | B           | B          | B           | B          |             |             |              |             | -0.60        | 0.13         |              |
| Tyr | 336 |              |             |             |            | B           | B          |             |             |              |             | -0.60        | 0.11         |              |
| Ile | 337 |              |             |             |            | B           | B          |             |             |              |             | -0.60        | 0.11         |              |
| Cys | 338 |              |             |             |            | B           | B          |             |             |              |             | -0.60        | 0.11         |              |
| Leu | 339 |              |             |             |            | B           | B          |             |             |              |             | -0.60        | 0.11         |              |
| Gly | 340 |              |             |             |            | B           | B          |             |             |              |             | -0.20        | 0.24         |              |
| Ala | 341 |              |             |             |            | B           | B          |             |             |              |             | -0.20        | 0.43         |              |
| Asn | 342 |              |             |             |            | B           | B          |             |             |              |             | 0.00         | 0.52         |              |
| Thr | 343 |              |             |             |            | B           | B          |             |             |              |             | 0.00         | 0.82         |              |
| Met | 344 |              |             |             |            | B           | B          |             |             |              |             | -0.45        | 1.09         |              |
| Gly | 345 |              |             |             |            | B           | B          |             |             |              |             | -0.80        | 0.59         |              |
| Tyr | 346 |              |             |             |            | B           | B          |             |             |              |             | -0.60        | 0.80         |              |
| Ser | 347 |              |             |             |            | B           | B          |             |             |              |             | -0.15        | 1.08         |              |
| Phe | 348 |              |             |             |            | B           | B          |             |             |              |             | -0.15        | 1.11         |              |
| Arg | 349 |              |             |             |            | B           | B          |             |             |              |             | -0.50        | 0.61         |              |
| Ser | 350 |              |             |             |            | B           | B          |             |             |              |             | -0.60        | 0.38         |              |
| Ala | 351 |              |             |             |            | B           | B          |             |             |              |             | -0.60        | 0.63         |              |

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| Res | Pos | Carni-<br>Alpha | Chou-<br>Alpha | Carni-<br>Beta | Chou-<br>Beta | Carni-<br>Turn | Chou-<br>Turn | Garni-<br>Coil | Kyte-<br>Hydro | Eisen-<br>Alpha | Eisen-<br>Beta | Karp-<br>Flexi | James-<br>Antig. | Emini-<br>Surfa |
|-----|-----|-----------------|----------------|----------------|---------------|----------------|---------------|----------------|----------------|-----------------|----------------|----------------|------------------|-----------------|
| Phe | 352 |                 |                | B              | B             |                |               |                | -1.47          | *               |                |                | -0.60            | 0.24            |
| Leu | 353 |                 |                | B              | B             |                |               |                | -0.98          | *               |                |                | -0.60            | 0.15            |
| Thr | 354 |                 |                | B              | B             |                |               |                | -1.09          |                 |                |                | -0.60            | 0.22            |
| Val | 355 |                 |                | B              | B             |                |               |                | -1.00          |                 |                |                | -0.60            | 0.43            |
| Leu | 356 |                 |                | B              | B             |                |               |                | -0.37          |                 |                |                | 0.10             | 0.81            |
| Pro | 357 |                 |                | B              | B             |                |               |                | 0.12           |                 |                |                | 1.74             | 1.12            |
| Asp | 358 |                 |                | B              | B             |                |               |                | 0.93           |                 |                |                | 2.08             | 2.33            |
| Pro | 359 |                 |                | B              | B             |                |               |                | 0.90           |                 |                |                | 2.52             | 4.90            |
| Lys | 360 |                 |                | B              | B             |                |               |                | 1.54           |                 |                |                | 2.66             | 3.14            |
| Pro | 361 |                 |                | B              | B             |                |               |                | 2.14           |                 |                |                | 3.40             | 2.90            |
| Gln | 362 |                 |                | B              | B             |                |               |                | 1.50           |                 |                |                | 2.76             | 2.90            |
| Cys | 363 |                 |                | B              | B             |                |               |                | 0.91           |                 |                |                | 2.02             | 1.08            |
| Pro | 364 |                 |                | B              | B             |                |               |                | 0.82           |                 |                |                | 0.93             | 0.70            |
| Ala | 365 |                 |                | B              | B             |                |               |                | 0.48           |                 |                |                | 0.39             | 0.55            |
| Val | 366 |                 |                | B              | B             |                |               |                | 0.39           |                 |                |                | 0.05             | 0.74            |
| Pro | 367 |                 |                | B              | B             |                |               |                | 0.49           |                 |                |                | 0.25             | 0.64            |
| Ser | 368 |                 |                | B              | B             |                |               |                | -0.16          |                 |                |                | -0.34            | 0.55            |
| Ser | 369 |                 |                | B              | B             |                |               |                | -0.26          |                 |                |                | -0.34            | 0.75            |
| Ser | 370 |                 |                | B              | B             |                |               |                | -0.34          |                 |                |                | -0.30            | 1.08            |
| Ser | 371 |                 |                | B              | B             |                |               |                | -0.26          |                 |                |                | 0.08             | 0.66            |
| Ala | 372 |                 |                | B              | B             |                |               |                | -0.34          |                 |                |                | 0.09             | 0.77            |
| Thr | 373 |                 |                | B              | B             |                |               |                | -0.38          |                 |                |                | 0.18             | 0.60            |
| Ser | 374 |                 |                | B              | B             |                |               |                | -0.38          |                 |                |                | 0.18             | 0.92            |
| Leu | 375 |                 |                | B              | B             |                |               |                | -0.38          |                 |                |                | 0.27             | 0.47            |
| Pro | 376 |                 |                | B              | B             |                |               |                | -0.93          |                 |                |                | 0.02             | 0.47            |

FIG. 40

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| Res | Pos | Garni_Alpha | Chou_Alpha | Garni_Beta | Chou_Beta | Garni_Turn | Chou_Turn | Garni_Coil | Chou_Coil | Kyte_Hydro | Eisen_Alpho | Eisen_Beta | Korpi_Flex | James_Antiq. | Emini_Surf_a |
|-----|-----|-------------|------------|------------|-----------|------------|-----------|------------|-----------|------------|-------------|------------|------------|--------------|--------------|
| Trp | 377 | B           | B          | B          | B         | T          | T         | -1.23      | -1.27     | -1.85      | *           | *          | -0.11      | 0.26         |              |
| Pro | 378 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.20      | 0.22         |              |
| Val | 379 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.60      | 0.14         |              |
| Val | 380 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.60      | 0.09         |              |
| Ile | 381 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.60      | 0.09         |              |
| Gly | 382 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.40      | 0.13         |              |
| Ile | 383 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.40      | 0.17         |              |
| Pro | 384 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.20      | 0.25         |              |
| Ala | 385 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.20      | 0.19         |              |
| Gly | 386 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.20      | 0.23         |              |
| Ala | 387 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.20      | 0.10         |              |
| Val | 388 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.60      | 0.09         |              |
| Phe | 389 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.60      | 0.09         |              |
| Ile | 390 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.60      | 0.12         |              |
| Gly | 391 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.60      | 0.14         |              |
| Thr | 392 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.60      | 0.13         |              |
| Leu | 393 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.60      | 0.15         |              |
| Leu | 394 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.60      | 0.19         |              |
| Leu | 395 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.60      | 0.06         |              |
| Leu | 396 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.60      | 0.13         |              |
| Trp | 397 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.60      | 0.15         |              |
| Leu | 398 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.60      | 0.32         |              |
| Cys | 399 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.20      | 0.61         |              |
| Gln | 400 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | -0.42      | 1.49         |              |
| Ala | 401 | B           | B          | B          | B         | B          | B         | -1.26      | -1.26     | -1.63      | *           | *          | 1.02       | 1.19         |              |

FIG. 4P

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| Res | Pas | Garni - Alpha | Chou - Alpha | Garni - Beta | Chou - Beta | Garni - Turn | Chou - Turn | Garni - Coil | Kyte - Hydro | Eisen - Alpha | Eisen - Beta | Eisen - Gamma | Korpi - Flexi | James - Antig. | Emini - Surfa - |
|-----|-----|---------------|--------------|--------------|-------------|--------------|-------------|--------------|--------------|---------------|--------------|---------------|---------------|----------------|-----------------|
| Gln | 402 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Lys | 403 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Lys | 404 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Pro | 405 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Cys | 406 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Thr | 407 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Pro | 408 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Ala | 409 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Pro | 410 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Ala | 411 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Pro | 412 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Pro | 413 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Leu | 414 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Pro | 415 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Cly | 416 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| His | 417 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Arg | 418 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Pro | 419 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Pro | 420 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Cly | 421 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Thr | 422 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Ala | 423 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Leu | 424 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Asp | 425 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Arg | 426 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |
| Ser | 427 |               |              |              |             |              |             |              |              |               |              |               |               |                |                 |

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| Res | Pos | Garni - Alpha | Garni - Beta | Garni - Chou - Beta | Garni - Chou - Turn | Garni - Chou - Coil | Kyle - Hydro - Alpha | Kyle - Hydro - Beta | Eisen - Alpha | Eisen - Beta | Karpl - Flexi | Jones - Antig. | Emini - Surfa |
|-----|-----|---------------|--------------|---------------------|---------------------|---------------------|----------------------|---------------------|---------------|--------------|---------------|----------------|---------------|
| Gly | 428 |               |              |                     |                     |                     |                      |                     | 1.39          | *            |               |                | 3.32          |
| Asp | 429 |               |              |                     |                     |                     |                      |                     | 1.98          | *            |               |                | 1.40          |
| Lys | 430 |               |              |                     |                     |                     |                      |                     | 1.69          | *            |               |                | 1.61          |
| Asp | 431 |               |              |                     |                     |                     |                      |                     | 0.77          | *            |               |                | 2.18          |
| Leu | 432 |               |              |                     |                     |                     |                      |                     | 0.48          | *            |               |                | 1.08          |
| Pro | 433 |               |              |                     |                     |                     |                      |                     | 0.23          | *            |               |                | 0.55          |
| Ser | 434 |               |              |                     |                     |                     |                      |                     | -0.58         |              |               |                | 0.33          |
| Leu | 435 |               |              |                     |                     |                     |                      |                     | -0.92         |              |               |                | 0.33          |
| Ala | 436 |               |              |                     |                     |                     |                      |                     | -1.51         |              |               |                | -0.06         |
| Ala | 437 |               |              |                     |                     |                     |                      |                     | -1.04         |              |               |                | -0.23         |
| Leu | 438 |               |              |                     |                     |                     |                      |                     | -1.04         |              |               |                | 0.22          |
| Ser | 439 |               |              |                     |                     |                     |                      |                     | -1.08         |              |               |                | -0.40         |
| Ala | 440 |               |              |                     |                     |                     |                      |                     | -1.13         |              |               |                | 0.40          |
| Gly | 441 |               |              |                     |                     |                     |                      |                     | -0.89         |              |               |                | 0.39          |
| Pro | 442 |               |              |                     |                     |                     |                      |                     | -1.11         |              |               |                | 0.35          |
| Gly | 443 |               |              |                     |                     |                     |                      |                     | -0.97         |              |               |                | 0.21          |
| Val | 444 |               |              |                     |                     |                     |                      |                     | -0.67         |              |               |                | 0.11          |
| Gly | 445 |               |              |                     |                     |                     |                      |                     | -0.08         |              |               |                | 0.26          |
| Leu | 446 |               |              |                     |                     |                     |                      |                     | -0.23         |              |               |                | 0.35          |
| Cys | 447 |               |              |                     |                     |                     |                      |                     | 0.10          |              |               |                | 0.22          |
| Glu | 448 |               |              |                     |                     |                     |                      |                     | 0.14          |              |               |                | 0.41          |
| Glu | 449 |               |              |                     |                     |                     |                      |                     | 0.79          |              |               |                | 0.67          |
| His | 450 |               |              |                     |                     |                     |                      |                     | 0.54          |              |               |                | 1.92          |
| Gly | 451 |               |              |                     |                     |                     |                      |                     | 0.77          |              |               |                | 1.12          |
| Ser | 452 |               |              |                     |                     |                     |                      |                     | 1.22          |              |               |                | 0.65          |
| Pro | 453 |               |              |                     |                     |                     |                      |                     | 1.22          |              |               |                | 0.74          |

FIG. 4R

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| Res | Pos | Garni - Alpha | Chou - Alpha | Garni - Beta | Chou - Beta | Garni - Turn | Chou - Turn | Garni - Coil | Chou - Coil | Eisen - Alpha | Eisen - Beta | Korpi - Flexi | James - Antig. | Emini - Surface |
|-----|-----|---------------|--------------|--------------|-------------|--------------|-------------|--------------|-------------|---------------|--------------|---------------|----------------|-----------------|
|     | 454 | A             | A            | B            | B           | -            | -           | C            | C           | 1.19          | 0.41         | F             | 0.88           | 1.30            |
| Ala | 455 |               |              |              |             |              |             |              |             | -0.06         | -0.10        | F             | 0.34           | 1.32            |
| Pro | 456 |               |              | A            | B           |              |             |              |             | -0.10         | -0.14        | F             | -0.45          | 0.70            |
| Gln | 457 |               |              | A            | B           |              |             |              |             | -0.10         | -0.14        | F             | -0.60          | 0.57            |
| His | 458 |               |              | A            | B           |              |             |              |             | -0.10         | -0.14        | F             | -0.60          | 0.56            |
| Leu | 459 |               |              | A            | B           |              |             |              |             | -0.10         | -0.14        | F             | -0.60          | 0.32            |
| Leu | 460 |               |              | A            | B           |              |             |              |             | -0.10         | -0.14        | F             | -0.60          | 0.32            |
| Gly | 461 |               |              | A            | B           |              |             |              |             | -0.12         | -0.12        | F             | -0.05          | 0.37            |
| Pro | 462 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 0.15           | 0.35            |
| Gly | 463 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 0.15           | 0.40            |
| Pro | 464 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 0.25           | 0.40            |
| Val | 465 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 0.45           | 0.40            |
| Ala | 466 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 0.65           | 0.81            |
| Gly | 467 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 0.45           | 0.43            |
| Pro | 468 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 0.35           | 0.92            |
| Lys | 469 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 1.00           | 1.40            |
| Leu | 470 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 1.80           | 2.85            |
| Tyr | 471 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 2.00           | 1.51            |
| Pro | 472 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 1.20           | 1.18            |
| Lys | 473 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 0.70           | 2.07            |
| Leu | 474 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 0.80           | 2.21            |
| Tyr | 475 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 0.20           | 1.00            |
| Thr | 476 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | -0.15          | 0.68            |
| Asp | 477 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | -0.45          | 1.19            |
| Ile | 478 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 0.56           | 1.03            |
| His | 479 |               |              | B            | B           |              |             |              |             | -0.12         | -0.12        | F             | 1.33           | 1.03            |

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| Res | Pos | Garni - Alpha | Chou - Alpha | Garni - Beta | Chou - Beta | Garni - Turn | Chou - Turn | Garni - Coil | Chou - Coil | Kyle - Hydro | Eisen - Alpha | Eisen - Beta | Korpl - Flexi | Jones - Aning | Emini - Surface |
|-----|-----|---------------|--------------|--------------|-------------|--------------|-------------|--------------|-------------|--------------|---------------|--------------|---------------|---------------|-----------------|
| Thr | 480 |               |              | B            | B           |              |             |              |             | 1.27         |               |              |               | -0.30         | 0.84            |
| His | 481 |               |              |              | B           |              |             | C            | C           | 1.54         |               |              |               | -0.25         | 1.74            |
| Thr | 482 |               |              |              |             |              |             | C            | C           | 1.24         |               |              |               | -0.25         | 1.74            |
| His | 483 |               |              |              |             |              |             | C            | C           | 2.10         |               |              |               | 0.45          | 1.61            |
| Thr | 484 |               |              |              |             |              |             | C            | C           | 1.82         |               |              |               | 0.45          | 1.61            |
| His | 485 |               |              |              |             |              |             | C            | C           | 2.10         |               |              |               | 0.45          | 1.61            |
| Ser | 486 |               |              |              |             |              |             | C            | C           | 1.80         |               |              |               | 0.45          | 1.50            |
| His | 487 |               |              |              |             |              |             | C            | C           | 2.11         |               |              |               | 0.45          | 1.50            |
| Thr | 488 |               |              |              |             |              |             | C            | C           | 1.29         |               |              |               | 0.51          | 0.83            |
| His | 489 |               |              |              |             |              |             | C            | C           | 1.60         |               |              |               | 0.87          | 1.06            |
| Ser | 490 |               |              |              |             |              |             | C            | C           | 1.29         |               |              |               | 1.33          | 0.72            |
| His | 491 |               |              |              |             |              |             | C            | C           | 1.63         |               |              |               | 1.99          | 1.06            |
| Val | 492 |               |              |              |             |              |             | C            | C           | 0.81         |               |              |               | 2.10          | 0.59            |
| Glu | 493 |               |              |              |             |              |             | B            | B           | 1.08         |               |              |               | 1.69          | 0.59            |
| Gly | 494 |               |              |              |             |              |             | B            | B           | 1.12         |               |              |               | 1.63          | 1.37            |
| Lys | 495 |               |              |              |             |              |             | B            | B           | 1.39         |               |              |               | 1.17          | 1.08            |
| Val | 496 |               |              |              |             |              |             | B            | B           | 0.53         |               |              |               | -0.09         | 0.76            |
| His | 497 |               |              |              |             |              |             | B            | B           | 1.36         |               |              |               | -0.30         | 0.52            |
| Cln | 498 |               |              |              |             |              |             | B            | B           | 1.11         |               |              |               | -0.45         | 1.10            |
| His | 499 |               |              |              |             |              |             | B            | B           | 1.46         |               |              |               | -0.60         | 0.43            |
| Ile | 500 |               |              |              |             |              |             | B            | B           | 0.74         |               |              |               | -0.20         | 0.41            |
| His | 501 |               |              |              |             |              |             | B            | B           | 1.21         |               |              |               | -0.20         | 0.74            |
| Tyr | 502 |               |              |              |             |              |             | B            | B           | 0.86         |               |              |               | -0.60         | 0.70            |
| Cln | 503 |               |              |              |             |              |             | B            | B           | 0.47         |               |              |               | 0.11          |                 |
| Cys | 504 |               |              |              |             |              |             | B            | B           |              |               |              |               |               |                 |

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

|   |  |   |
|---|--|---|
| Applicant's or agent's file reference<br>4239-55911                                       | <b>FOR FURTHER ACTION</b>                                | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
| International application No.<br>PCT/US00/26689   | International filing date (day/month/year)<br>29/09/2000 | Priority date (day/month/year)<br>02/10/1999  |
| International Patent Classification (IPC) or national classification and IPC<br>C07K14/00 |  |   |
| Applicant<br>THE GOVERNMENT OF THE UNITED STATES OF AMERICA, as                           |  |   |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

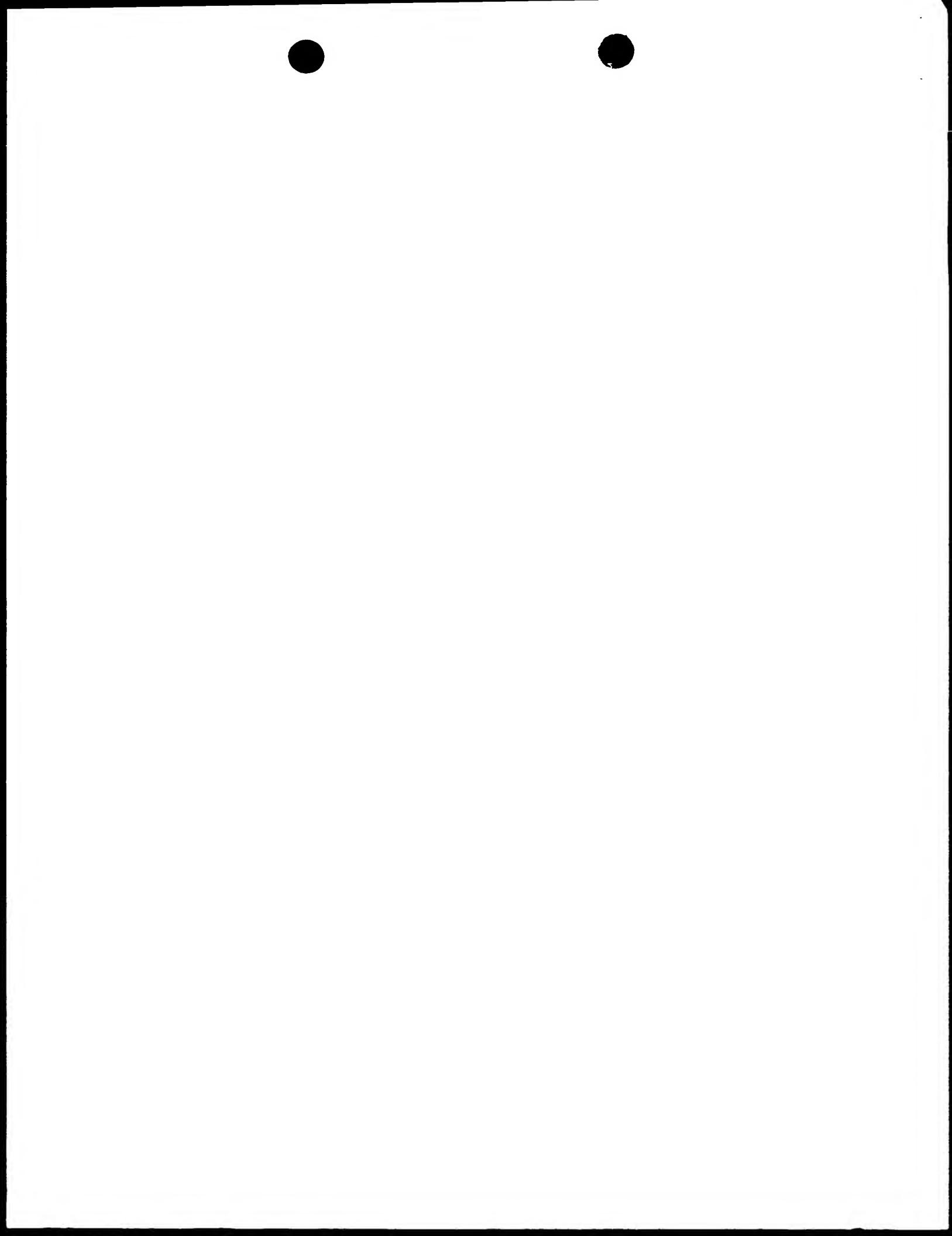
These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I     Basis of the report
- II     Priority
- III     Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV     Lack of unity of invention
- V     Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI     Certain documents cited
- VII     Certain defects in the international application
- VIII     Certain observations on the international application

|  |   |
|--|---|
| Date of submission of the demand<br>30/04/2001   | Date of completion of this report<br>18.12.2001                       |
| Name and mailing address of the international preliminary examining authority:<br><br><br>European Patent Office - Gitschner Str. 103<br>D-10958 Berlin<br>Tel. +49 30 25901 - 0<br>Fax: +49 30 25901 - 840 | Authorized officer<br><br>Siatou, E<br>Telephone No. +49 30 25901 327 |





**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/26689

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-71 as originally filed

**Claims, No.:**

1-41 as originally filed

**Drawings, sheets:**

1/8-8/8 as originally filed

**Sequence listing part of the description, pages:**

1-17, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

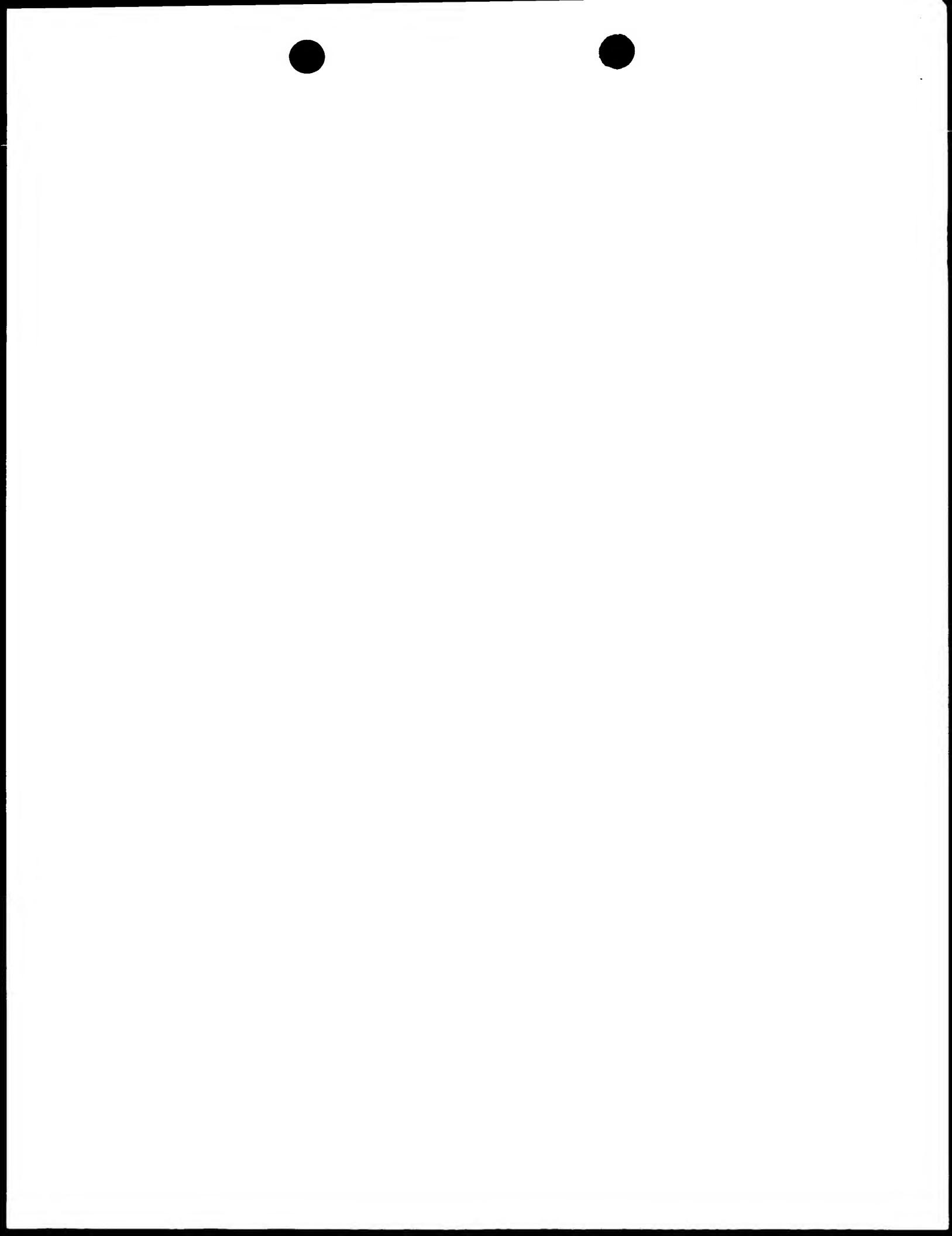
These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:



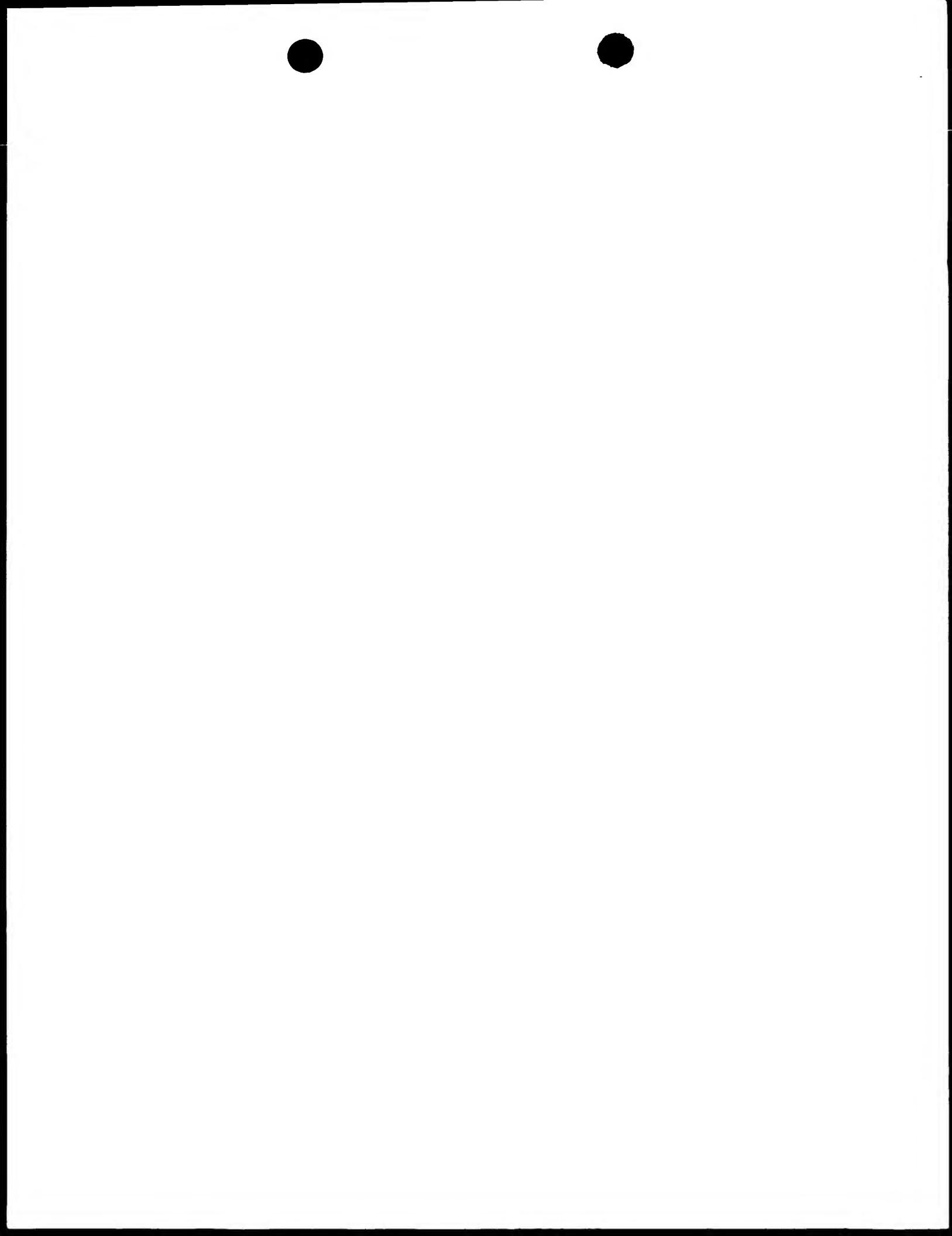
**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/26689

- the description,      pages:  
 the claims,      Nos.:  
 the drawings,      sheets:
5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)): *(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*
6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- the entire international application.
- claims Nos. 1-26, 37-41 and 27-32(partially) in respect of industrial applicability.
- because:
- the said international application, or the said claims Nos. 1-26, 37-41 and 27-32 (partially) in respect of industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos. 1-5, 17, 20-21, 23, 25-26, 33-38 (all partially).
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- the written form has not been furnished or does not comply with the standard.
- the computer readable form has not been furnished or does not comply with the standard.



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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

1. Statement

|                     |      |                           |
|---------------------|------|---------------------------|
| Novelty (N)         | Yes: | Claims 7-22, 25-32, 40-41 |
|                     | No:  | Claims 1-6, 23-24, 33-39  |
| Inventive step (IS) | Yes: | Claims 7-22, 25-32, 40-41 |
|                     | No:  | Claims 1-6, 23-24, 33-39  |

Industrial applicability (IA)

|      |                          |
|------|--------------------------|
| Yes: | Claims 27-32 (partially) |
| No:  | Claims                   |

2. Citations and explanations  
**see separate sheet**

**VI. Certain documents cited**

1. Certain published documents (Rule 70.10)

and / or

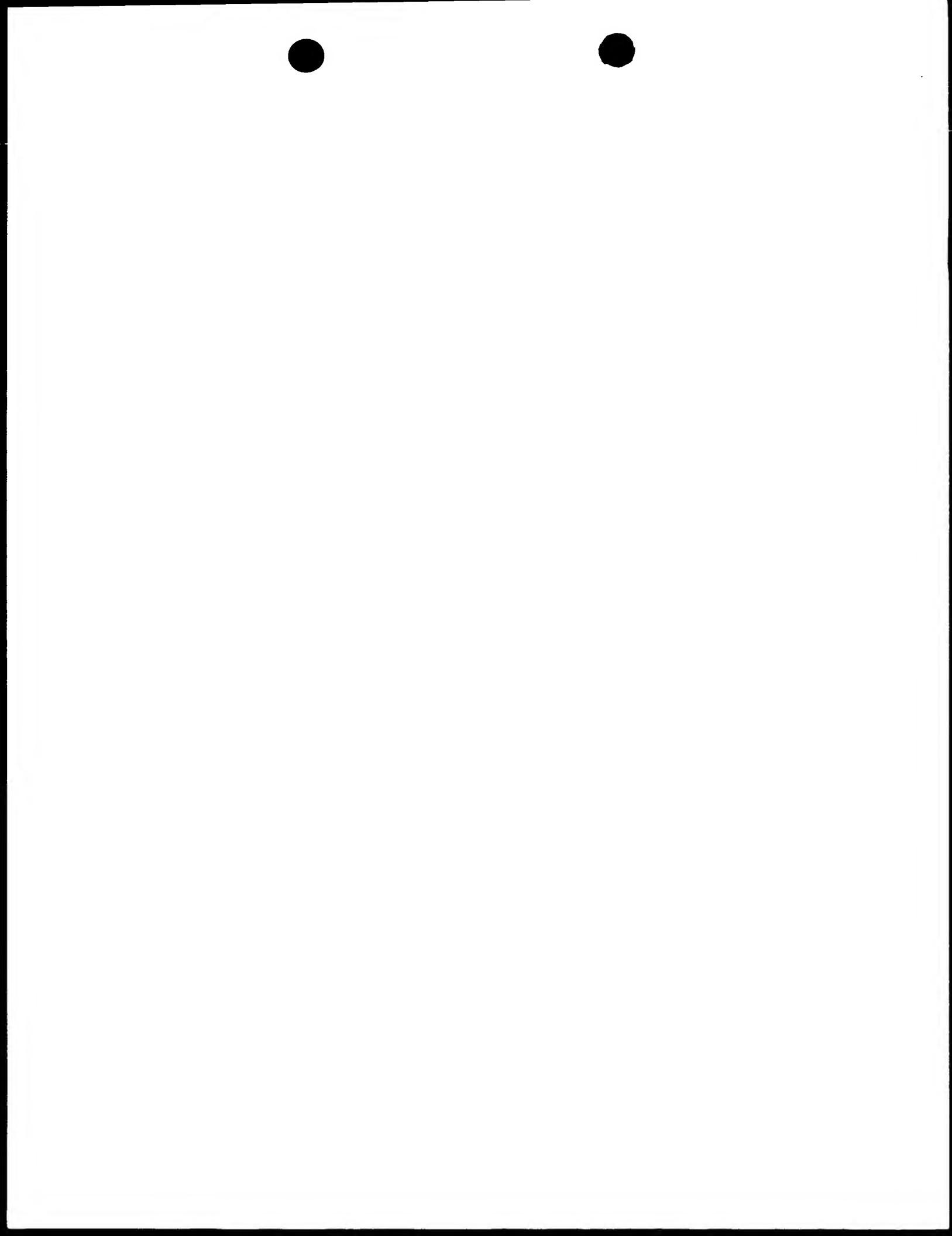
2. Non-written disclosures (Rule 70.9)

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**



**Re Item III**

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 1-26, 27-32, as far as in vivo applications are concerned, and 37-41 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

2. An opinion will be given for those parts of the application which have been the subject of a search report, namely the parts relating to the use of FGF-5 polypeptides, nucleic acids encoding FGF-5, FGF-5 antisense molecules, antibodies to FGF-5 and immunoreactive sensitized T cells sensitized with FGF-5.

**Re Item V**

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The Applicant's attention is drawn to the fact that the present opinion expressed as to the novelty, inventive step and industrial applicability refers only to the matter for which an international search report has been drawn up.

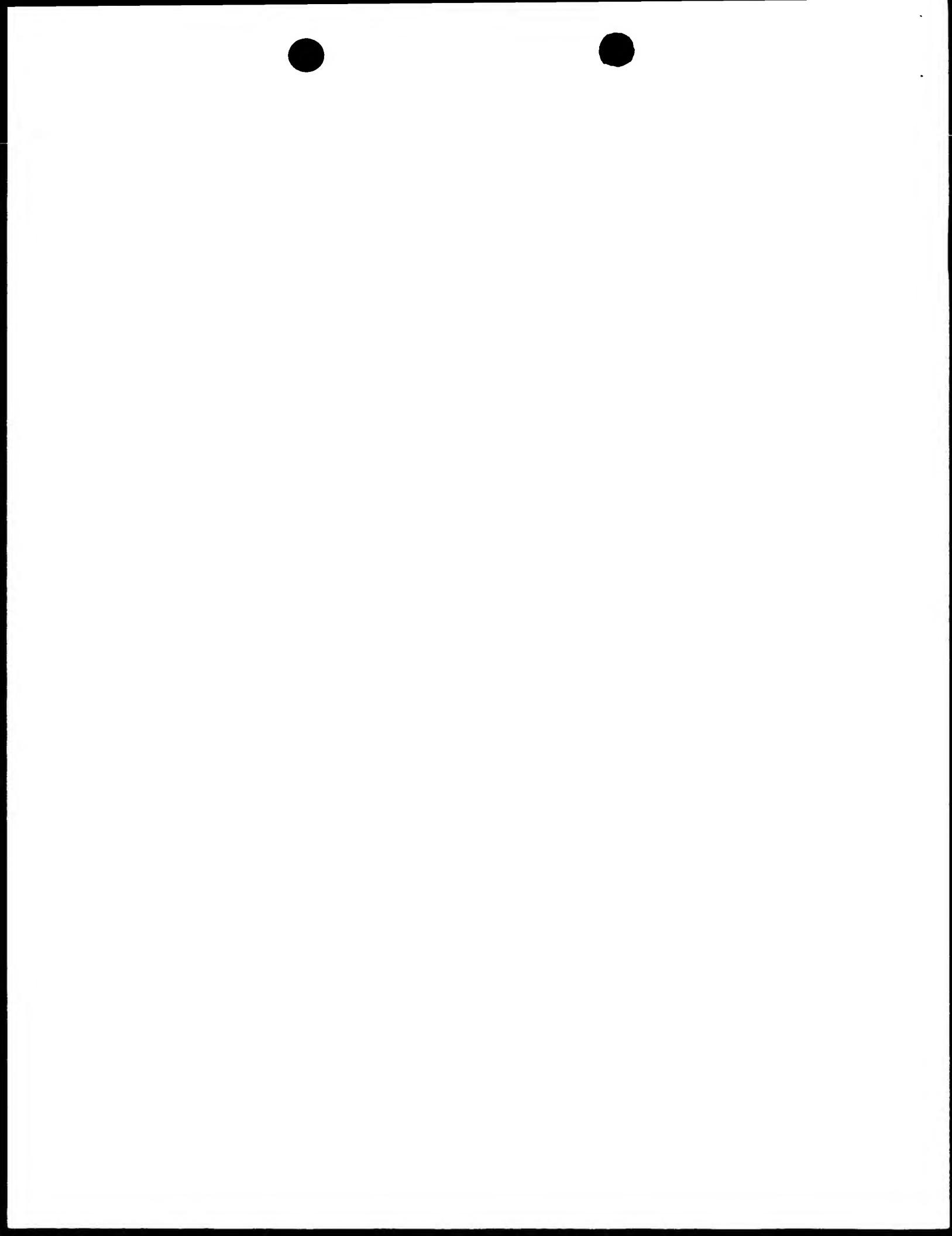
Reference is made to the following documents:

D1: WO-A-9012597

D2: JP-A-10017599 (PAJ abstract)

Document D1 discloses pharmaceutical compositions comprising a conjugate of fibroblast growth factor (FGF) or a polypeptide reactive with an FGF receptor and a cytotoxic agent for treating a variety of FGF-mediated diseases, such as tumors. FGF-5 is explicitly mentioned (see claims 1-21 and page 5, lines 13-34). The subject matter of claims 1-6, 23-24 and 37-39 of the present invention is neither novel nor inventive (Art. 33(2) and 33(3) PCT).

Document D2 (see abstract) discloses antibodies binding exclusively to FGF-5 and



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/26689

their use in detecting the presence of FGF-5. The subject matter of claims 33-36 is neither novel nor inventive (Art. 33(2) and 33(3) PCT).

None of the cited prior art documents discloses or suggests the subject matter of claims 7-22, 25-32 and 40-41. The subject matter of these claims meets the requirements of Art. 33(2) and 33(3) PCT.

**Re Item VI**

Certain documents cited

Certain published documents (Rule 70.10)

Application No

Patent No      Publication date

(day/month/year)      Filing date

(day/month/year)      Priority date (valid claim)

(day/month/year)

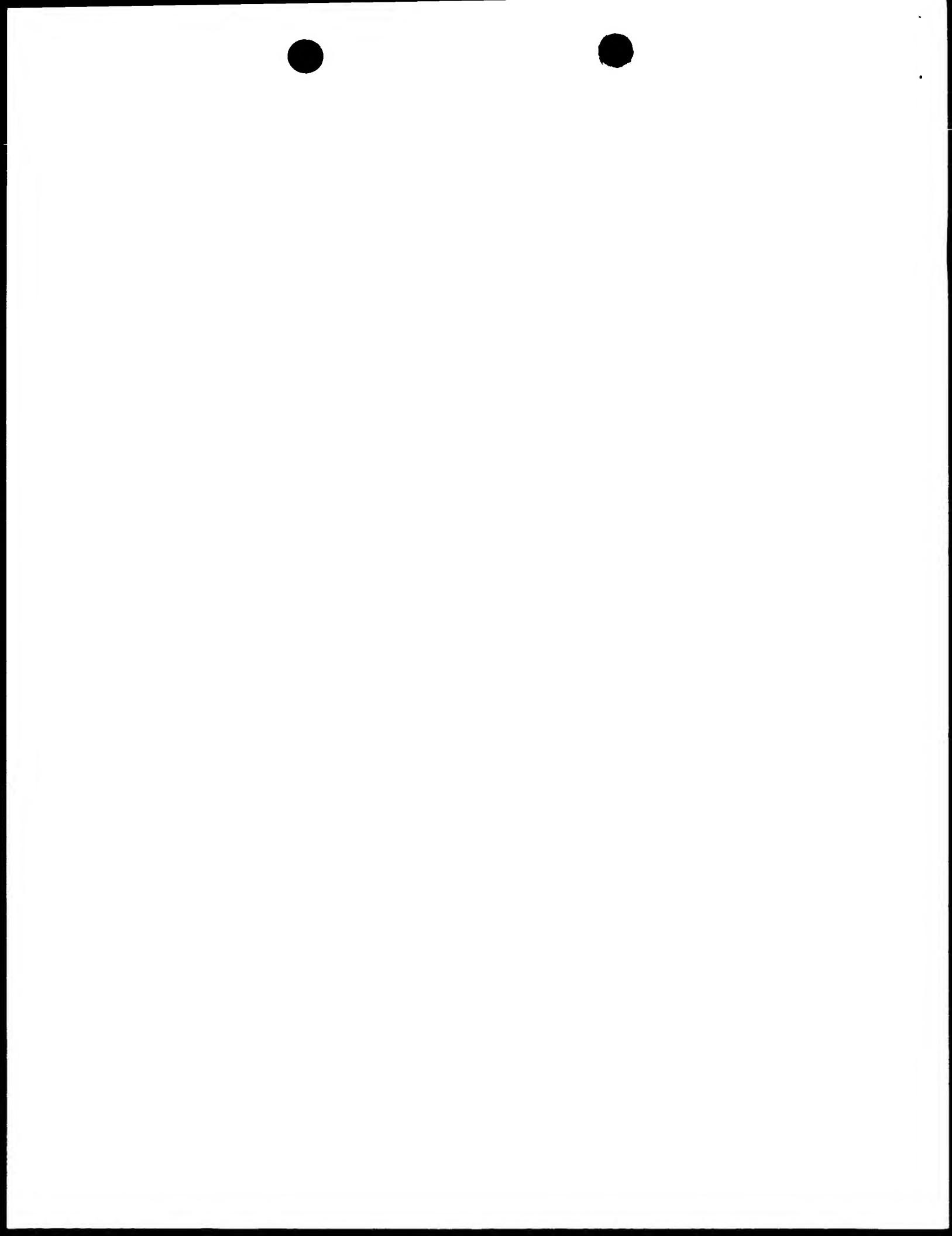
|              |          |          |          |
|--------------|----------|----------|----------|
| WO-A-0024756 | 04.05.00 | 17.06.99 | 23.10.98 |
| WO-A-9955861 | 04.11.99 | 15.04.99 | 28.04.98 |

**Re Item VIII**

Certain observations on the international application

Claim 1 does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claim attempts to define the subject-matter in terms of the result to be achieved which merely amounts to a statement of the underlying problem. The technical features necessary for achieving this result should be added.

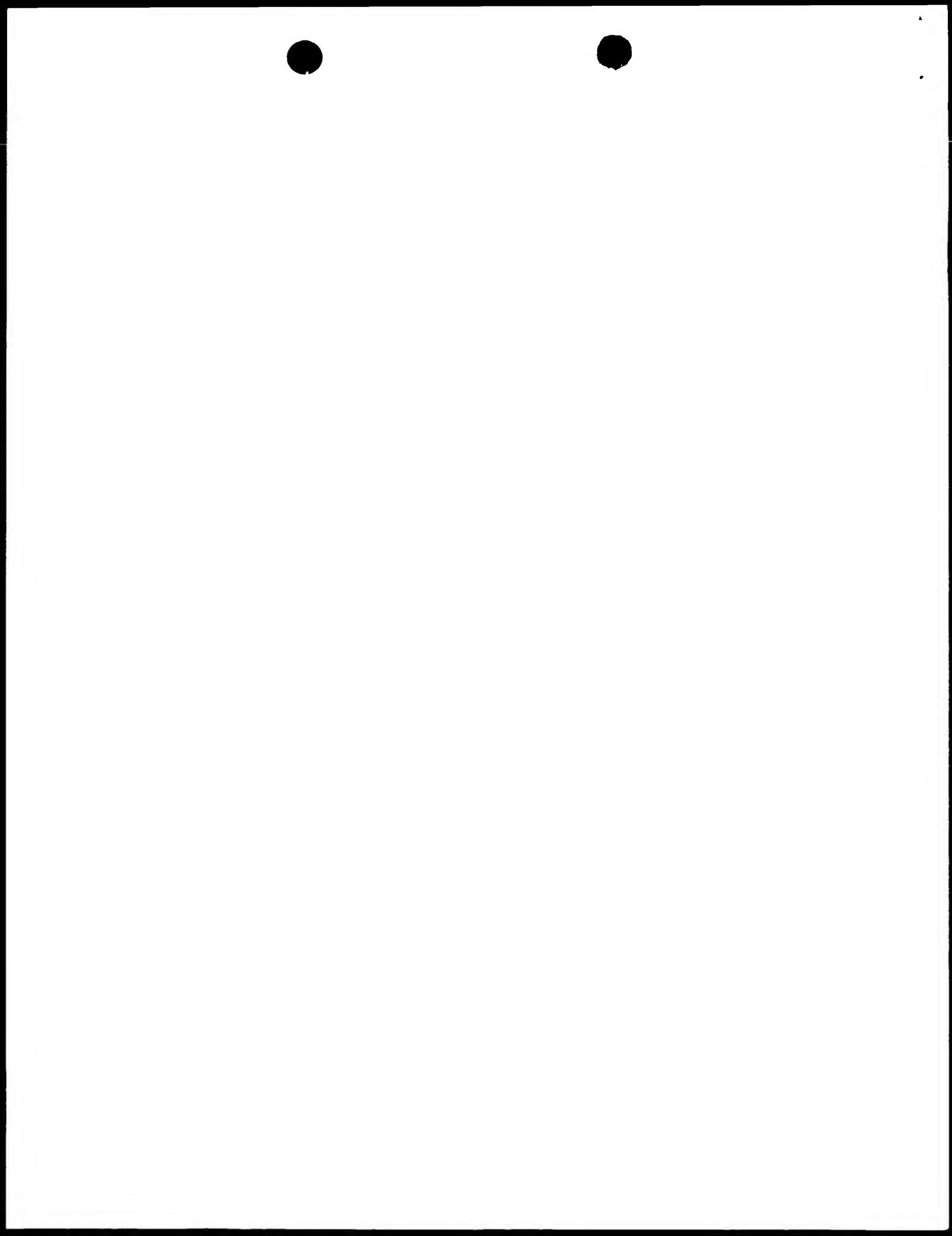
Moreover, and as already stated in the search phase, support within the meaning of Art. 6 PCT and/or disclosure within the meaning of Art. 5 PCT is to be found for only a very small number of compounds/products within the scope of the present application, namely use of FGF-5 polypeptides, nucleic acids encoding FGF-5, FGF-5 antisense molecules, antibodies to FGF-5 and immunoreactive sensitized T cells sensitized with FGF-5.



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/US00/26689



## PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION  
(PCT Rule 61.2)Date of mailing (day/month/year)  
17 July 2001 (17.07.01)To:  
Commissioner  
US Department of Commerce  
United States Patent and Trademark  
Office, PCT  
2011 South Clark Place Room  
CP2/5C24  
Arlington, VA 22202  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

International application No.  
PCT/US00/26689Applicant's or agent's file reference  
4239-55911International filing date (day/month/year)  
29 September 2000 (29.09.00)Priority date (day/month/year)  
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## Applicant

HANADA, Ken-Ichi et al

1. The designated Office is hereby notified of its election made:

 in the demand filed with the International Preliminary Examining Authority on:

30 April 2001 (30.04.01)

 in a notice effecting later election filed with the International Bureau on:

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2. The election
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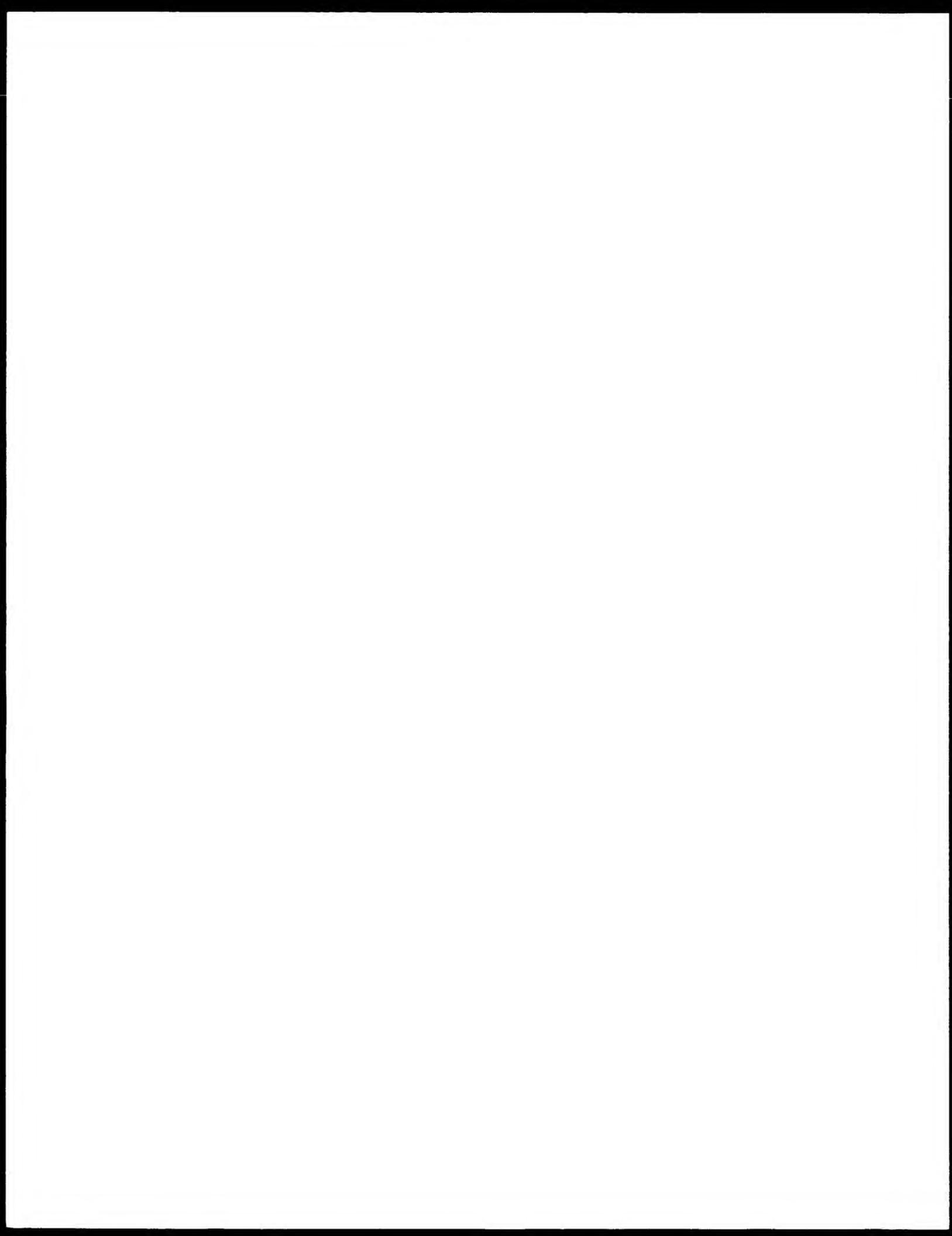
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Telephone No.: (41-22) 338.83.38



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(74) **Agent:** NOONAN, William, D., Klarquist, Sparkman, Campbell, Leigh & Whinston, LLP, One World Trade Center, Suite 1600, 121 SW Salmon Street, Portland, OR 97204 (US)

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(71) **Applicant (for all designated States except US): THE GOVERNMENT OF THE UNITED STATES OF AMERICA, as represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES [US/US]:** The National Institutes of Health, Office of Technology Transfer, Suite 325, 6011 Executive Boulevard, Rockville, MD 20852-3804 (US).

(72) Inventors; and

(75) **Inventors/Applicants** (for US only): **HANADA, Ken-Ichi** [JP/US]; 10101 Grosvenor Place, #1209, Rockville, MD 20852 (US). **YANG, James, C.** [US/US]; 1 Serpentine Court, Silver Spring, MD 20904 (US).

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WO 01/25271 A3

(54) Title: FIBROBLAST GROWTH FACTOR-5 (FGF-5) IS A TUMOR ASSOCIATED T-CELL ANTIGEN

**(57) Abstract:** Disclosed herein are methods for treating tumors which express or over-express the tumor associated antigen (TAA) fibroblast growth factor 5 (FGF-5), including renal cell carcinoma (RCC) and carcinoma of the prostate and breast. Methods include modulating an immune response, such as increasing an immune response, or modulating FGF-5 expression or activity. The disclosure also includes methods of determining if a subject has an enhanced susceptibility to a disease associated with abnormal FGF-5 expression.

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 00/26689

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 A61K38/18 C07K14/50 A61K39/395 C07K16/22

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
 IPC 7 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and where practical search terms used)

EPO-Internal, CHEM ABS Data, EMBASE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category * | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No                        |
|------------|--|---|
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Further documents are listed in the continuation of box C

Patent family members are listed in annex.

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Date of the actual completion of the international search

Date of mailing of the international search report

9 July 2001

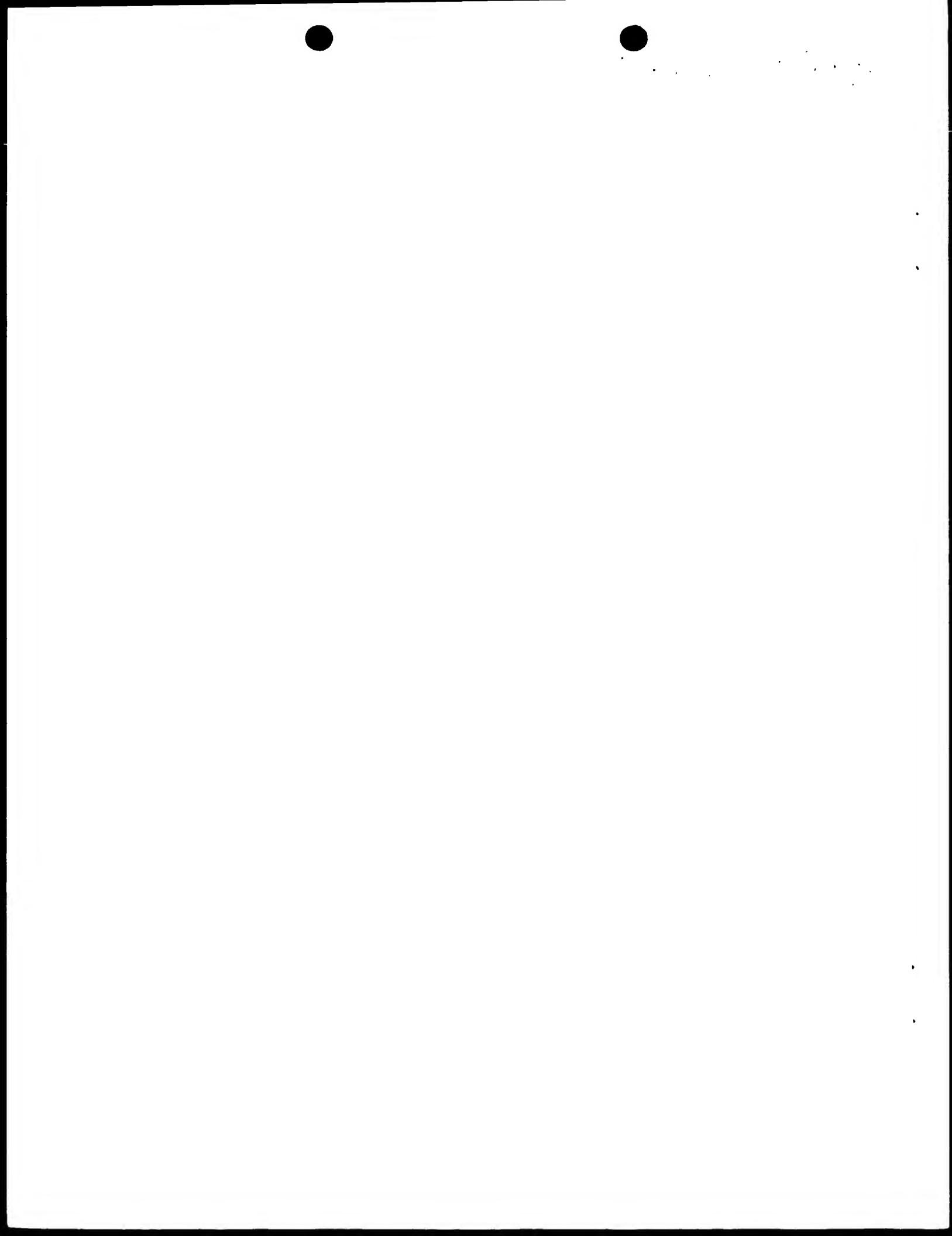
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European Patent Office, P.O. Box 5818 Patentlaan 2  
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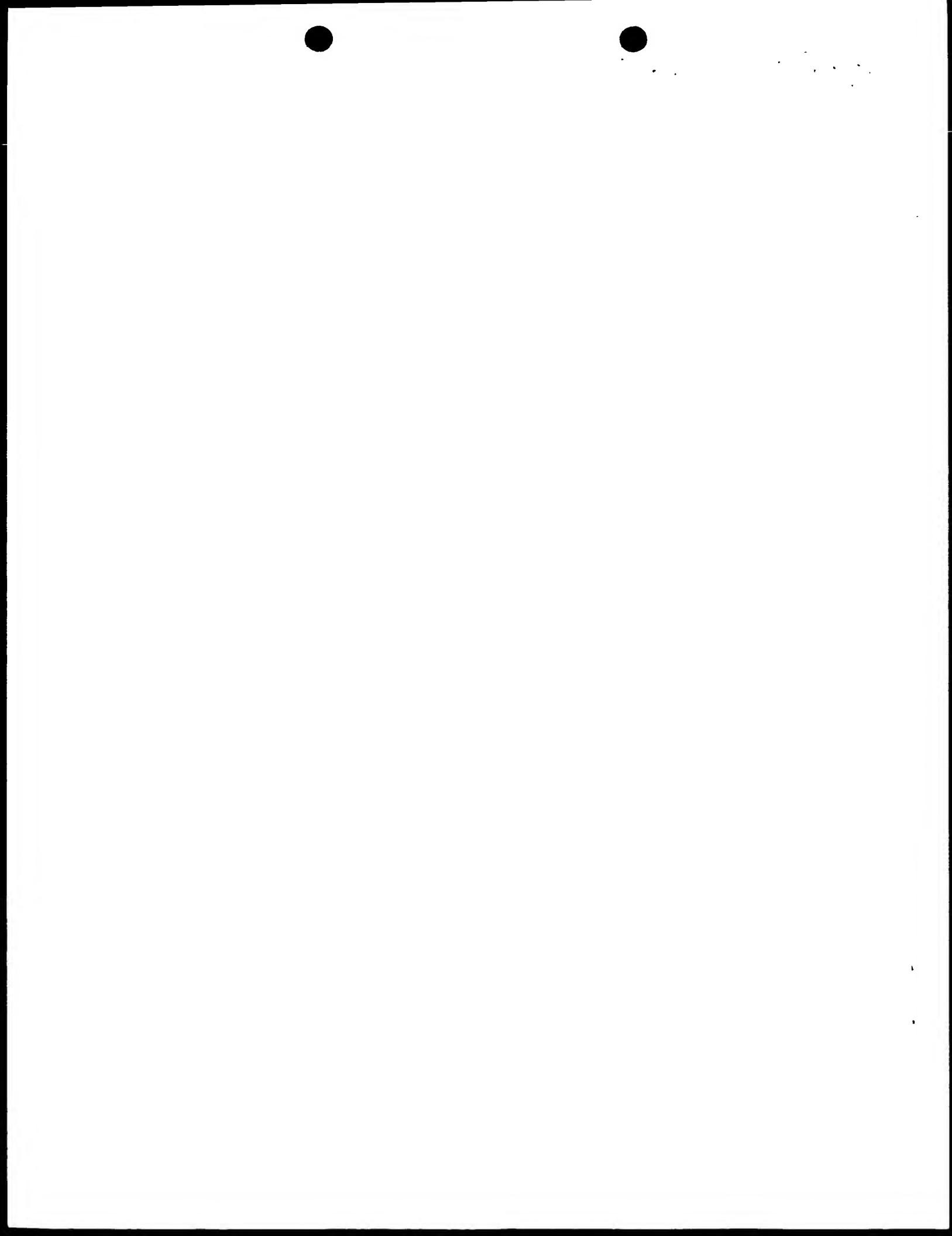
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## INTERNATIONAL SEARCH REPORT

|                              |
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| International Application No |
| PCT/US 00/26689              |

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT |   |                      |
|--|---|----------------------|
| Category   | Citation of document, with indication where appropriate of the relevant passages  | Relevant to claim No |
| X  | PATENT ABSTRACTS OF JAPAN<br>vol. 1998, no. 05,<br>30 April 1998 (1998-04-30)<br>& JP 10 017599 A (POLA CHEM IND INC),<br>20 January 1998 (1998-01-20)<br>abstract<br>---   | 33-36                |
| A  | ZHAN X ET AL: "THE HUMAN FGF-5 ONCOGENE<br>ENCODES A NOVEL PROTEIN RELATED TO<br>FIBROBLAST GROWTH FACTORS"<br>MOLECULAR AND CELLULAR<br>BIOLOGY, US, WASHINGTON, DC,<br>vol. 8, no. 8, 1 August 1988 (1988-08-01),<br>pages 3487-3495, XP002034597<br>ISSN: 0270-7306<br>abstract<br>---   | 1-41                 |
| A  | DATABASE EMBASE 'Online'<br>ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM,<br>NL;<br>YAMANAKA K. ET AL: "Expression of<br>fibroblast growth factors in human<br>non-papillary renal cell carcinoma:<br>Correlation with tumor progression."<br>retrieved from STN<br>Database accession no. 1999207619<br>XP002171451<br>abstract<br>& INTERNATIONAL JOURNAL OF CLINICAL<br>ONCOLOGY, (1999) 4/2 (74-77). ,<br>---           | 1-41                 |
| A  | DATABASE CHEMABS 'Online'<br>CHEMICAL ABSTRACTS SERVICE, COLUMBUS,<br>OHIO, US;<br>YOSHIMURA, KOJI ET AL: "Messenger<br>ribonucleic acids for fibroblast growth<br>factors and their receptor in bladder and<br>renal cell carcinoma cell lines"<br>retrieved from STN<br>Database accession no. 124:339650 HCA<br>XP002171452<br>abstract<br>& CANCER LETT. (SHANNON. IREL.) (1996),<br>103(1), 91-7 .<br>---<br>-/- | 1-41                 |

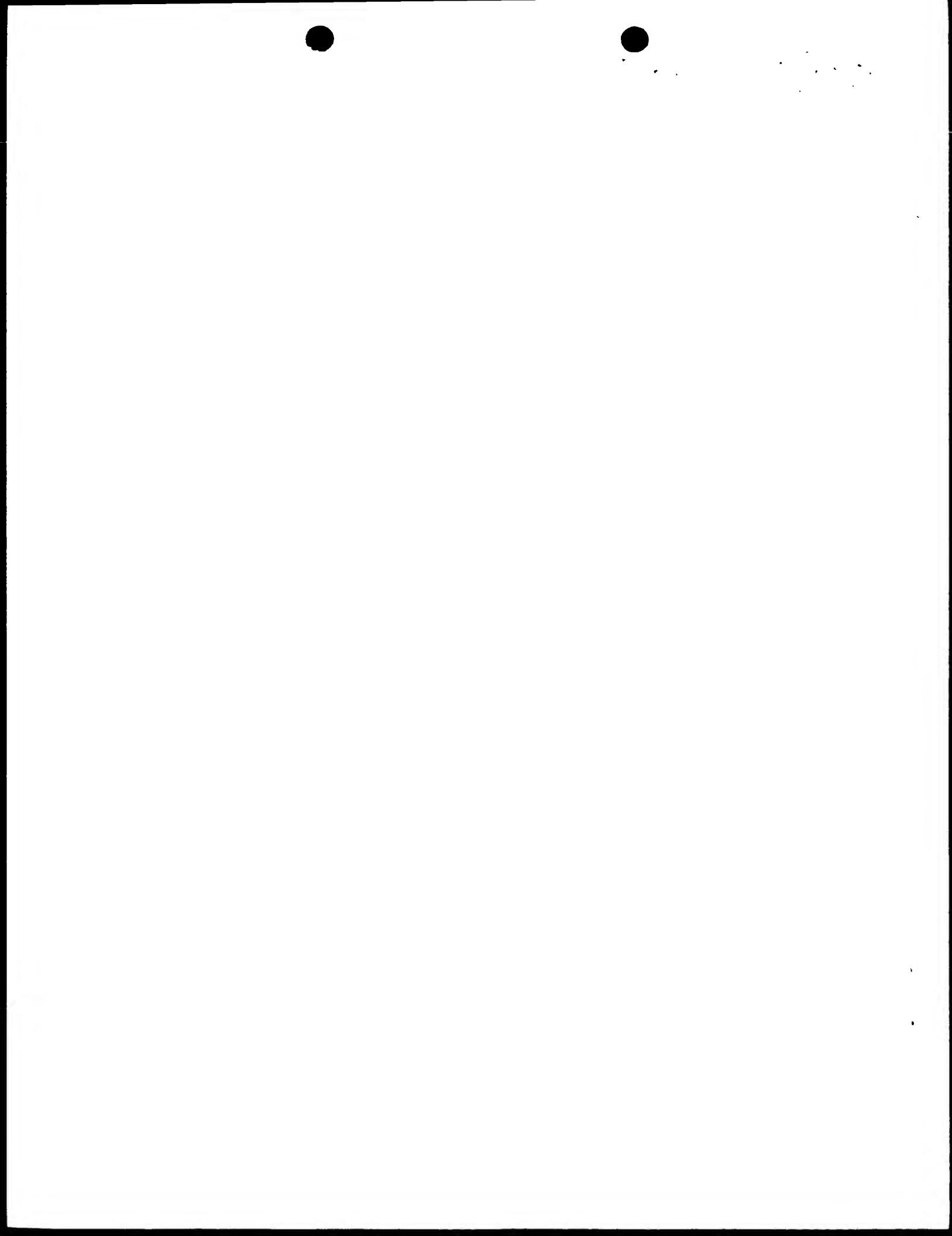


## INTERNATIONAL SEARCH REPORT

Internal Application No  
PCT/US 00/26689

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication where appropriate of the relevant passages  | Relevant to claim No |
|----------|---|----------------------|
| A        | DATABASE CHEMABS 'Online!<br>CHEMICAL ABSTRACTS SERVICE. COLUMBUS,<br>OHIO, US;<br>WERNER, SABINE ET AL: "Fibroblast growth<br>factor 5 proto-oncogene is expressed in<br>normal human fibroblasts and induced by<br>serum growth factors"<br>retrieved from STN<br>Database accession no. 116:35063 HCA<br>XP002171453<br>abstract<br>& ONCOGENE (1991), 6(11), 2137-44 ,<br>----- | 1-41                 |



FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 1-26, 37-41 and 27-32, as far as they refer to an *invivo* method, are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

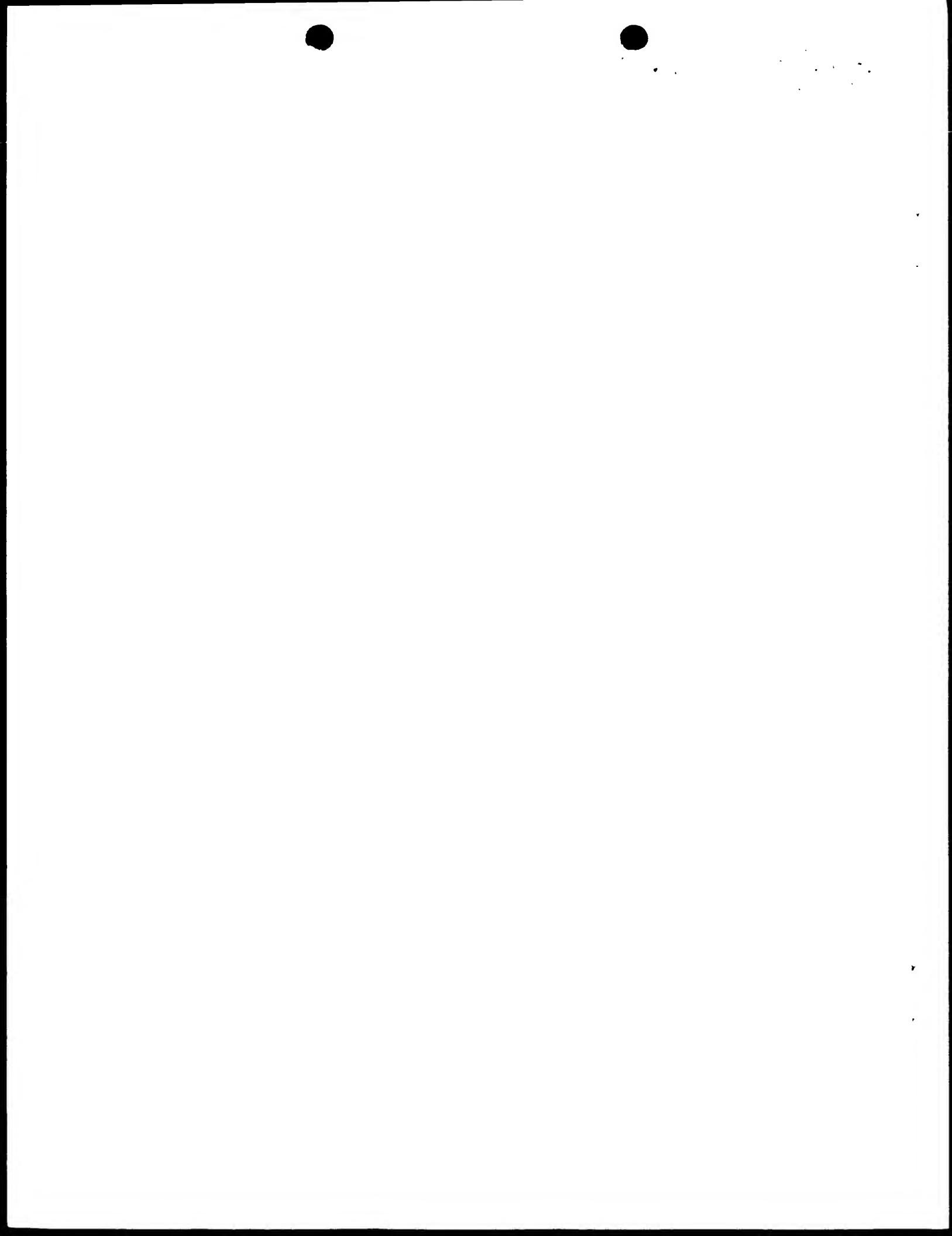
Although claims 33-36 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.2

Present claims 1-5, 17, 20-21, 23, 25-26, 33-38 relate to a compound defined by reference to a desirable characteristic or property, namely modulation of FGF-5 expression/activity or modulation of immune response to FGF-5.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the use of FGF-5 polypeptides, nucleic acids encoding FGF-5, FGF-5 antisense molecules, antibodies to FGF-5 and immunoreactive sensitized T cells sensitized with FGF-5.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.



## INTERNATIONAL SEARCH REPORT

Information on patent family members

| International Application No |
|------------------------------|
| PCT/US 00/26689              |

| Patent document cited in search report |   | Publication date |    | Patent family member(s) |  | Publication date |
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